Prediction of Intervention Effects in Health Systems: Johns Hopkins HealthCare Diabetes Case Study

by

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Abstract

We use administrative, claims, and clinical data from Johns Hopkins HealthCare (JHHC) to investigate (1) plan members' health states and health state trajectories, and (2) optimal interventions to improve population health at more affordable costs. Our study population consists of 56,349 members, 27,636 (49%) of whom have an ICD-10 diabetes diagnosis.

We use a simulation-based approach to predict intervention effects and their uncertainty. Our prediction of intervention effects (PIE) model is composed of seven component models corresponding to member enrollment, health state, probability of positive expenditure, size of positive expenditure, and disenrollment due to death, changing plan, or other reasons. We apply our PIE model to two interventions targeted to diabetic members: (1) reducing the effect of diabetes on health state and expenditure by 0-5% and (2) reducing patients' plasma glucose concentration (HbA1c) by 0-1%.

We find that diabetic patients have worse health states, higher probability of positive expenditure, and greater magnitude positive expenditure than otherwise similar non-diabetic patients. Diabetic members have lower hazard of disenrollment due to death, changing plan given survival, and disenrolling for other reasons given survival and not changing plan than otherwise similar non-diabetic patients.

In our first intervention, we predict $60 in monthly savings per diabetic member if we reduce the effect of diabetes on both health state and expenditure by 2.5%. In our second intervention, we predict $200 in monthly savings per Medicare Advantage member if we reduce HbA1c by 0.7%.

We propose our PIE model as a decision-support tool to quantitatively evaluate the relative merits of different interventions. One of its strengths is its flexibility; the component models can be adapted to the scientific question of interest without changing the overarching PIE model structure.

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Chapter 1

Introduction

1.1 Precision Medicine

Societies have practiced medicine for millennia. In its earliest forms, the distinction between medicine, magic, and religion was poorly defined. Various ailments, now understood to have biological explanations, were ascribed to curses cast by the Gods. Treatments were crude and sometimes did more harm than good. Ancient Greek physician Hippocrates was the first to propose that medical conditions have natural, rather than supernatural, explanations. He coined the maxim, "first, do no harm" (*primum non nocere*) and is credited by many with developing the theory of the four humours. He proposed that the four humours—blood, yellow bile, black bile, and phlegm—could explain all bodily functions and dysfunctions. This theory advocated for such practices as bloodletting when the physician believed a patient's condition was due to an overabundance of blood and thus a systemic imbalance. Despite Hippocrates' fundamental belief in a physician's obligation to do no harm, bloodletting was generally more detrimental than beneficial to the patient.

Throughout history, physicians have sought to tailor their medical care to the individual; they have used their judgment to prescribe the treatment they believe will yield the best therapeutic benefit. However, even physicians with the best of intentions are not infallible. As history has shown, their judgments can be inadequately supported by data and sometimes misguided. Medicine has evolved beyond measure between Hippocrates' life and now—life expectancy is increasing, cancer survival rates are improving, and diagnostic tools are more sensitive, among other metrics of improvement. Individualized medicine is entering its latest iteration: precision medicine. Precision medicine uses all available data to provide the best supported behavioral and medical interventions. Best medical practice should be continually refined as indicated by new data so that patients can attain their best possible outcomes and live their best possible lives.

1.2 National Healthcare Expenditure

The Organization for Economic Cooperation and Development (OECD) was established in 1961 to encourage international collaboration and problem-solving. There are 36 OECD countries, including the United States, that cooperate to develop data-driven policy recommendations. The OECD countries are international leaders in economic, social, and health policy and will be referenced to contextualize health expenditure and health outcomes in the United States.

The United States spent $3.5 trillion on healthcare in 2017 (OECD, 2017). National healthcare expenditure is predicted to grow by 5.5% per year through 2027 (CMS, 2017). Despite ever-increasing costs, health outcomes have not improved to match. The US is falling behind other OECD countries in myriad health measures while outpacing them in expenditure (Sawyer and McDermott, 2019). More than concerning, the trend is unsustainable as national healthcare expenditure is growing more rapidly than the economy. The US spent 17.2% of GDP on healthcare in 2017 (Figure 1.1). It is predicted to reach 19.4% by 2026 (Cuckler et al., 2018).

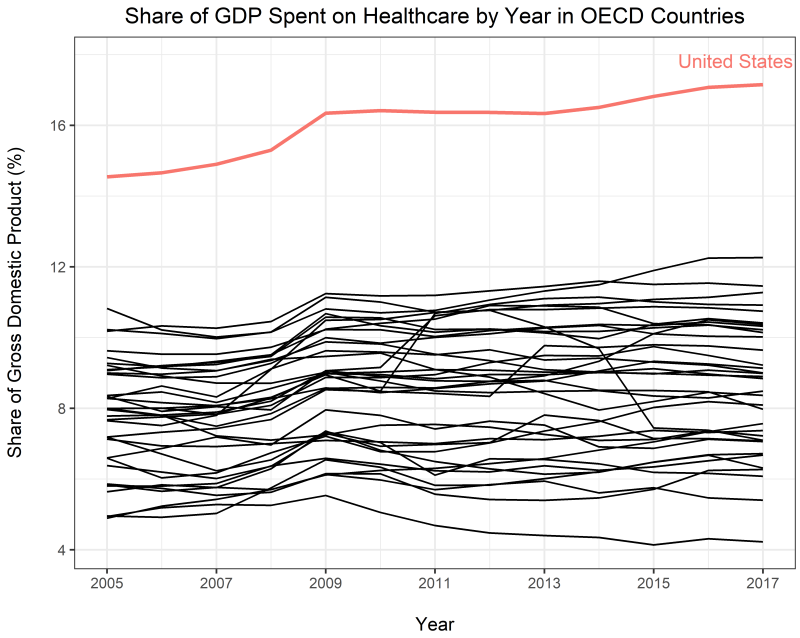

Figure 1.1: Percent of GDP spent on healthcare in OECD countries from 2005 to 2017. The US has consistently spent the largest percent of GDP on healthcare out of the OECD countries. The OECD countries with the next highest percent GDP spent on healthcare in 2017 are Switzerland, France, and Germany which spent 12.3, 11.5, and 11.3%, respectively (OECD, 2017).

The unchecked growth of national healthcare expenditure and the burden this places on patients and payers are not without hope. There is an estimated 34% waste in the healthcare expenditure (Berwick and Hackbarth, 2012), where waste is understood to be "outlays for health services that could be eliminated without harming consumers or care quality" (O'Neill and Scheinker, 2018). That 34% translates to over $1 trillion. Recovering even some fraction of this waste offers enormous opportunity to make quality healthcare more affordable for patients, providers, and payers. Further, such savings could be redirected to value-adding public policies that have historically been preempted by national healthcare costs.

1.3 Diabetes: A Public Health Crisis

1.3.1 Epidemiology

Diabetes is a metabolic disease in which the body produces little to no insulin or cannot effectively use insulin (NLM, 2019). Insulin is a hormone necessary to transport glucose—a major source of energy—from the blood stream to cells. When insulin is poorly regulated, patients are at risk for hyper- and hypoglycemia;[1] either imbalance can cause adverse systemic effects up to and including death (Mayo Clinic, 2019). In the long-term, poorly regulated blood sugar can lead to complications such as blindness and predispose diabetics to other conditions such as cardiovascular disease and kidney disease.

[1] Hyper- and hypoglycemia refer to high and low blood sugar, respectively.

The prevalence of diabetes has grown consistently since the 1950s. In 1958, less than 1% of the population had a diabetes diagnosis; by 2015 that number had risen to 7.4% (CDC, 2017a). Between 1980 and 2012, both the prevalence and incidence of diabetes doubled (Geiss et al., 2014). The latest reports estimate that 30.3 million people in the US have diabetes (9.4% of the population), 23.8% of whom do not know they have the disease (CDC, 2017b). The percent of people with diabetes increases with age; 25.2% of people over 65 have diabetes (CDC, 2017b).

These patterns are highly concerning for both the patient and payer. For the patient, the number of complications and coexisting conditions associated with diabetes can reduce both quality and length of life. In 2014, 7.2 million hospital discharges listed diabetes as one of the diagnoses; the primary reasons for these hospitalizations include major cardiovascular disease, lower-extremity amputation, and diabetic ketoacidosis (CDC, 2017b). There were an additional 14.2 million emergency room visits which listed diabetes as one of the diagnoses; approximately one third of these visits were due to hyper- or hypoglycemia (CDC, 2017b). For the payer, the concerns are obvious: diabetes and its associated complications, comorbidities, and hospitalizations compromise their member's health and are expensive.

1.3.2 Cost

The estimated cost of diabetes in 2012 was $245 billion (CDC, 2017b). Diabetic patients are estimated to have annual medical expenditure of $13,700, over half of which can be attributed to diabetes (CDC, 2017b). Insulin-dependent

diabetics cannot survive without insulin injections; however, the price of insulin nearly tripled between 2009 and 2017 from $92.70 to $274.70 (Kaiser Health News, 2019). Patients, especially those without medical insurance, are forced to make difficult decisions about what sacrifices they can make to afford their life-saving medication. Some are pushed to sell personal belongings and tap retirement funds to pay for their prescriptions (Prasad, 2019) or, in extreme cases, ration insulin which can lead to premature and preventable death (Sable-Smith, 2018). The cost of diabetes extends beyond dollars; it costs lives. Patients deserve evidence-based interventions to improve their health at more affordable costs.

1.3.3 Interventions

Many risk factors for diabetes can be managed through behavioral interventions. Smoking, obesity, physical inactivity, and high blood pressure are all associated with increased risk of diabetes (CDC, 2017b). Interventions that encourage smoking cessation, diet, and exercise can delay or prevent development of diabetes as well as help manage symptoms in existing cases.

One such intervention is the National Diabetes Prevention Plan (National DPP). The National DPP was first evaluated in a randomized clinical trial lasting 2.8 years. 3,150 adults at high-risk for developing diabetes were randomized to lifestyle intervention, metformin,[2] or placebo. Those in the first group realized the greatest benefit with a 58% reduction in diabetes incidence

[2]Metformin is an oral medication used to treat high blood sugar. It promotes production of and sensitivity to insulin in the body. It is the most common treatment for non-insulin dependent diabetics.

as compared to placebo (Diabetes Prevention Program Research Group, 2009). An extended follow-up lasted for seven additional years; at the end of the extended follow-up (i.e. 10 years since randomization), those patients who were assigned to lifestyle intervention experienced a 34% reduction in cumulative incidence of diabetes as compared to placebo (Diabetes Prevention Program Research Group, 2009). The National DPP offers persisting benefits up to at least 10 years post-enrollment.

Chapter 2

Literature Review

2.1 Healthcare Expenditure Data

Healthcare expenditure data are often positively skewed. This pattern is driven by a few patients having very large medical expenditures relative to the majority of patients with more moderate, usual-care expenses. Additionally, healthcare expenditure data are often heteroscedastic. The variance tends to increase with increasing mean (Blough and Ramsey, 2000). Two common approaches to analyzing these data are log-linear models and two-part models (Duan et al., 1983).

Healthcare expenditure data can be analyzed using a log-linear model if the error terms after log-transformation are both Gaussian and homoscedastic. Predicted values from this approach are in terms of log dollars and need to be retransformed to obtain predicted values in dollars. This retransformation is accomplished by exponentiating predicted log dollars and multiplying by the retransformation factor $\exp\left\{\hat{\sigma}^2/2\right\}$ where $\hat{\sigma}^2$ denotes the estimated mean squared error (Duan et al., 1983).

Two-part models are used when the healthcare expenditure data have a large proportion of zeros; this happens when many individuals have no expenditure in at least one of the measurement intervals (Blough and Ramsey, 2000). Two-part models are based on mixed probability distributions and treat expenditure as arising from two processes: (1) the probability of a positive expenditure, and (2) the size of the expenditure conditioned on it being positive (Blough and Ramsey, 2000). The probability of a positive expenditure can be expressed as a probit model and the size of the expenditure conditioned on it being positive can be expressed as a log-linear model (Duan et al., 1983). The predicted expenditure is the product of the probability of positive expenditure, the size of the expenditure given it is positive, and the retransformation factor.

Duan proposes the smearing coefficient $\frac{1}{n}\sum_{i=1}^{n}\exp\{\hat{\varepsilon}_i\}$ as an alternative to the retransformation factor in log-linear regression (Duan, 1983).[1] The smearing coefficient can outperform the retransformation factor because $\exp\{x_0\hat{\beta}+\hat{\sigma}^2/2\}$ is not always consistent for $E[Y_0]$, where x_0 denotes the design matrix, $\hat{\beta}$ denotes the least squares regression coefficients, $\hat{\sigma}^2$ denotes the mean squared error, and Y_0 denotes the response.[2] Duan demonstrates that the smearing estimate $\frac{1}{n}\sum_{i=1}^{n}\exp\{x_0\hat{\beta}+\hat{\varepsilon}_i\}$ is consistent when the retransformation function is continuously differentiable. In the case of log-linear regression, the retransformation function is the exponential which is continuously differentiable; thus, the smearing estimate is consistent (Duan, 1983).

[1] The smearing coefficient can be used for other transformations but we will specifically discuss it with respect to log-transformation.

[2] $\exp\{x_0\hat{\beta}+\hat{\sigma}^2/2\}$ is consistent for $\exp\{x_0\beta+\sigma^2/2\}$ whether or not the error terms follow a Gaussian distribution. $\exp\{x_0\hat{\beta}+\hat{\sigma}^2/2\}$ may not be consistent for $E[Y_0]$ when the error terms do not follow a Gaussian distribution.

2.2 Causal Framework

Suppose we are interested in the causal effect of some exposure variable A on an outcome variable Y. Let A be a binary exposure variable where $A = 0$ when there is no exposure and $A = 1$ when there is an exposure. Then define $Y_{a=0}$ to be the outcome under exposure $a = 0$ and $Y_{a=1}$ to be the outcome under exposure $a = 1$ (Hernán, 2004). Hernán writes that the exposure A has a causal effect if $Y_{a=0} \neq Y_{a=1}$. This is the concept of an **individual causal effect** (Hernán, 2004). However, this definition presents what Holland terms the "Fundamental Problem of Causal Inference"; he writes that we cannot observe both $Y_{a=0}$ and $Y_{a=1}$ on the same unit and it is therefore impossible to observe the effect of A (Holland, 1986). There are various frameworks designed to address the Fundamental Problem of Causal Inference, such as the Rubin Causal Model. While the individual causal effect is inherently unobservable, the **average causal effect** can be estimated from the observed individual outcomes and is equal to $T = E[Y_{a=1} - Y_{a=0}]$ (Holland, 1986). However, estimating the average causal effect necessarily requires multiple units.

In this thesis, the unit of study is the Johns Hopkins HealthCare system (i.e. $N = 1$); we are interested in estimating the system-wide causal effect of various interventions. We cannot observe the system under both observed and intervention conditions. We propose a simulation-based approach to predict the causal effects of various interventions.

2.3 Restricted Latent Class Models

An individual's health state cannot be directly measured. However, observed clinical data can help to understand latent health state. One approach to modeling latent health state is to use Restricted Latent Class Models (RLCMs). Xu and Shang describe a family of RLCMs: suppose we collect J binary responses for a subject; these responses can be stored in a $J \times 1$ vector R. Assume that these responses can be explained by K binary latent attributes; these attributes can be stored in a $K \times 1$ vector α. Define a binary $K \times L$ Q-matrix that reflects known relationships between R and α (Xu and Shang, 2018). Wu et al. (2019) "define clusters to be comprised of those observations with identical latent states." Two individuals i and j would be in the same cluster if $\alpha_i = \alpha_j$. Wu et al. (2019) propose scientifically structured clustering as a Bayesian method to estimating these clusters when the Q-matrix and the number of distinct clusters are unknown. This approach can be used to cluster patients with shared latent health states. Prior knowledge from clinical data and the Johns Hopkins ACG system could be used to develop initial clusters (Johns Hopkins, 2019).

Chapter 3

A Brief Tour of the JHHC Data

We use monthly Johns Hopkins HealthCare (JHHC) data from July 2017 through June 2018. Our raw dataset includes every JHHC member with an ICD-10 diabetes diagnosis during this period ($n = 28,489$). It also includes two non-diabetic members for each diabetic member ($n = 56,920$). These non-diabetics were randomly sampled from the remaining JHHC member base ($n = 467,274$). Our resulting dataset includes $85,409$ members. Of these, we consider only persons who are 18 years of age or older and have nonzero Resource Utilization Band (RUB) scores (see section 3.2). After filtering by these criteria, there are $56,349$ patients in our study population, $27,636$ (49%) of whom have an ICD-10 diabetes diagnosis.

These patients are enrolled in one of JHHC's four lines of business: Employer Health Programs (EHP), Medicare Advantage (MA), Priority Partners (PP), and US Family Health Plan (USFHP) ("About Us"). The total number of members and member-months by line of business and diabetes diagnosis are summarized in Table 3.1 and Table 3.2.

Table 3.1: Non-diabetic and diabetic members by line of business

Line of Business	**Non-diabetic Members** Members (%)	**Diabetic Members** Members (%)	**Total** Members (%)
EHP	5,462 (9.7)	3,482 (6.2)	8,944 (15.9)
MA	1,123 (2.0)	3,578 (6.3)	4,701 (8.3)
PP	18,197 (32.3)	15,640 (27.8)	33,837 (60.0)
USFHP	3,931 (7.0)	4,936 (8.7)	8,867 (15.7)
Total	28,713 (51.0)	27,636 (49.0)	56,349 (100)

Table 3.2: Non-diabetic and diabetic member months by line of business

Line of Business	**Non-diabetic Members** Member months (%)	**Diabetic Members** Member Months (%)	**Total** Member Months (%)
EHP	53,521 (10.1)	33,030 (6.2)	86,551 (16.3)
MA	10,000 (1.9)	29,904 (5.6)	39,904 (7.5)
PP	172,666 (32.6)	139,481 (26.3)	312,147 (58.8)
USFHP	40,278 (7.6)	51,532 (9.7)	91,810 (17.3)
Total	276,465 (52.1)	253,947 (47.9)	530,412 (100)

MA has more than three diabetic patients to every one non-diabetic patient despite our overall study population having an approximately equal number of diabetic and non-diabetic patients. This feature makes it an interesting target for diabetes intervention programs. EHP has the opposite pattern with approximately one diabetic patient to every two non-diabetic patients. PP and USFHP have more balanced numbers of non-diabetics and diabetics.

MA has the fewest months of observation per individual (i.e. member months per member) and USFHP has the highest months of observation per individual. Diabetics tend to have somewhat fewer months of observation than their non-diabetic counterparts, except in USFHP. These patterns can be seen in Figure 3.1.

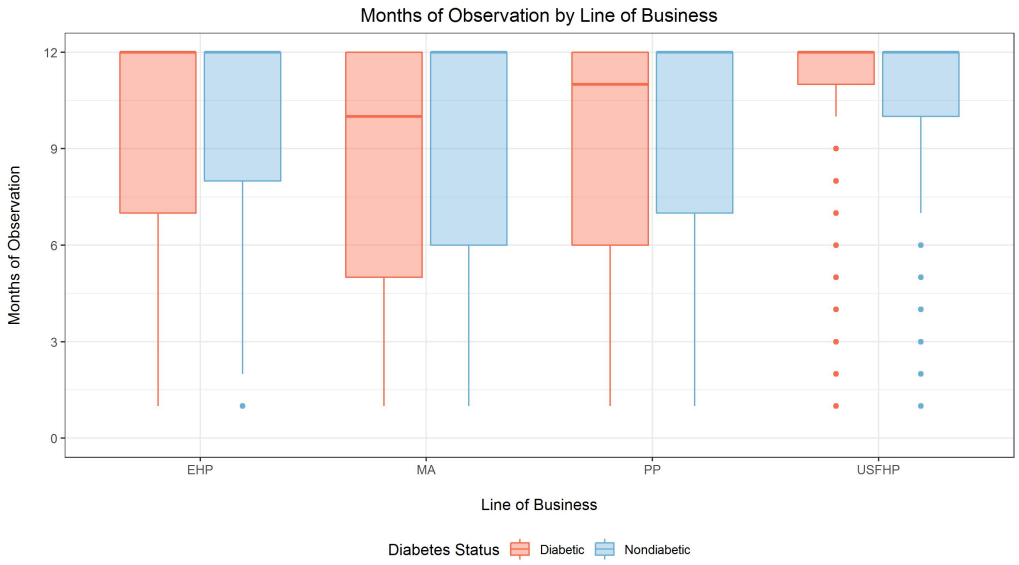

Figure 3.1: Months of observation by line of business and diabetes status. The median number of months of observation is 12 for non-diabetic patients in all lines of business. The median number of months of observation is 12, 10, 11, and 12 for diabetic patients in EHP, MA, PP, and USFHP, respectively. USFHP has the highest member retention.

3.1 Population Demographics

We did not match on age, sex, or plan when obtaining our representative sample of non-diabetics because we wanted it to be just that—representative. There are imbalances in the JHHC population and we wanted to maintain these so our predicted intervention effects are reflective of what might be attained in the true population.

Non-diabetic members tend to be younger than diabetic members (Figure 3.2); on average, non-diabetic members are 39.8 years old (sd = 16.1) and diabetic members are 55.3 years old (sd = 14.6) (Table 3.3). All subsequent analyses adjust for age so estimated diabetes effects are not an artifact of differing age distributions.

Figure 3.2: Age distribution by line of business and diabetes status.

PP members tend to be the youngest (mean age = 41.5), followed by EHP (mean age = 45.0), USFHP (mean age = 59.6), and MA (mean age = 70.8). These age differences have ramifications for each line of business as older members tend to have worse health states and higher expenditures (section 3.2, section 3.3).

Table 3.3: Non-diabetic and diabetic member age by line of business

Line of Business	**Non-diabetic Members** Mean (SD)	**Diabetic Members** Mean (SD)	**Total** Mean (SD)
EHP	39.8 (13.7)	53.2 (11.7)	45.0 (14.5)
MA	70.7 (9.7)	70.8 (8.7)	70.8 (8.9)
PP	35.4 (13.2)	48.7 (11.8)	41.5 (14.2)
USFHP	51.0 (17.8)	66.4 (12.9)	59.6 (17.1)
Total	39.8 (16.1)	55.3 (14.6)	47.4 (17.3)

3.2 Population Health

We have two measures of health state: (1) Resource Utilization Band (RUB) score as a macro-level measure of health state, and (2) plasma glucose concentration (HbA1c) as a micro-level measure of health state specific to estimating how well-controlled a case of diabetes is, if present.

3.2.1 Health State

We use RUB score as a proxy for health state. RUB scores are not derived from an individual's health data; rather, they are a measure of the extent to which an individual utilizes medical resources. An individual with a RUB score of 1 is a low utilizer and an individual with a RUB score of 5 is a high utilizer, with 2, 3, and 4, as intermediate and ordered levels of utilization. RUB score is an imperfect measure of health state. In subsection 6.2.2, we discuss future plans for improving this aspect of our approach as more clinical data are made available.

Diabetics obviously have poorer health states and higher RUB scores than otherwise similar non-diabetics. This can be seen in Figure 3.3; the proportion of non-diabetic members with RUB score 1 or 2 is greater than the proportion of diabetic members with RUB score 1 or 2 in all age strata. The same is true for RUB score 3 in all but the youngest age stratum (18-25 years of age). The pattern reverses for RUB scores 4 and 5, with a greater proportion of diabetic patients falling into these categories than non-diabetics in all age strata.

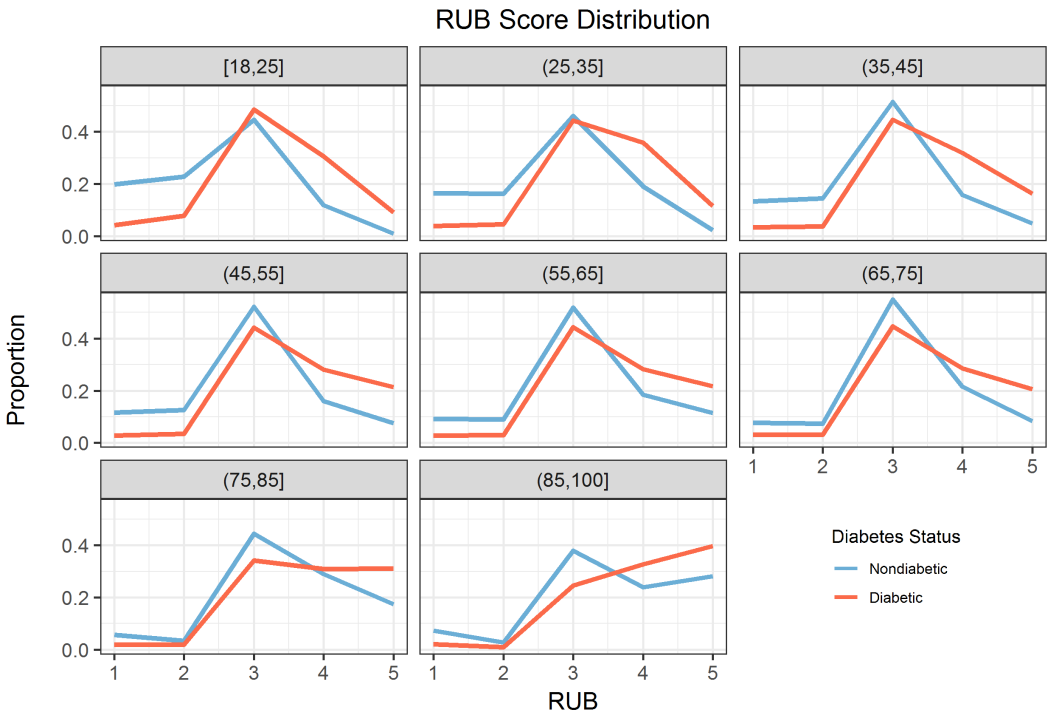

Figure 3.3: Proportion of population falling into each RUB score category by diabetes diagnosis and age. Age categories are displayed in the banner over each plot and show age in years.

3.2.2 Plasma glucose concentration (HbA1c)

We use plasma glucose concentration (HbA1c) as a clinically-grounded measure of diabetes health state. We have 10,964 member-months of HbA1c data out of 530,412 member-months (2%). HbA1c less than 5.7%, between 5.7-6.5%, and greater than 6.5% are diagnosed as non-diabetic, pre-diabetic, and diabetic, respectively (American Diabetes Association, 2019). In our study population, the median HbA1c measurements in non-diabetic, pre-diabetic, and diabetic patients are 5.4%, 6.1%, and 7.0%, respectively (Figure 3.4).

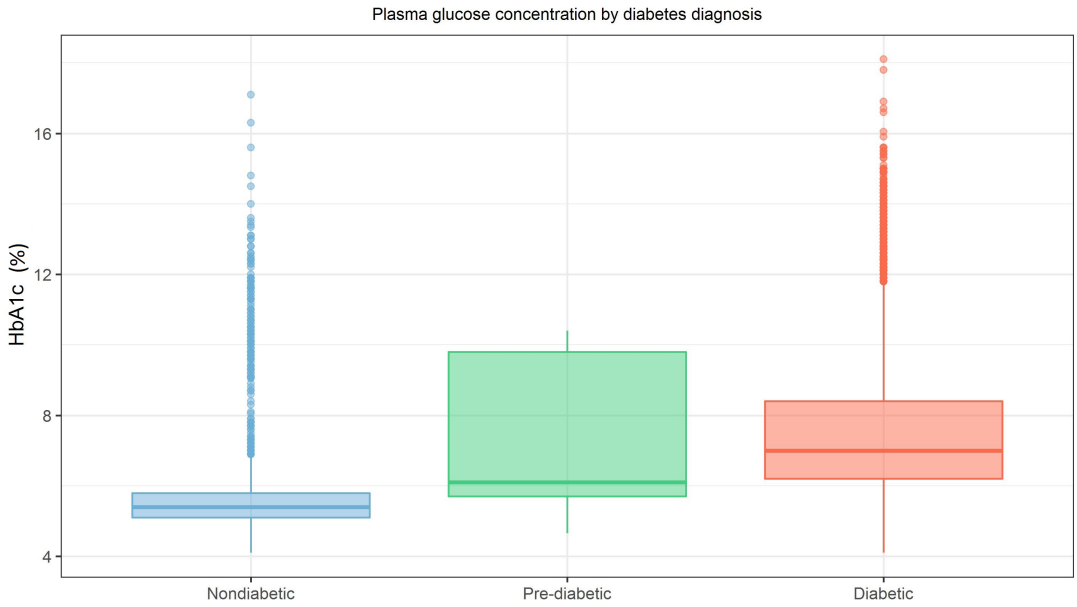

Figure 3.4: Plasma glucose concentration by diabetes diagnosis.

3.3 Population Expenditure

We explore patterns in "per member per month (PMPM)" expenditure where PMPM expenditure is defined to be average monthly expenditure per member. Figure 3.5 shows the relationship between diabetes, age, and PMPM expenditure. We see that there are more non-diabetics than diabetics in the three youngest age strata (18-25, 26-35, 36-45 years of age). Diabetics become more prevalent than non-diabetics at age 46-55 and remain so in all subsequent strata. We standardize the frequency plots to density plots to more clearly see the relative distributions of PMPM expenditure (Figure 3.6). Diabetic patients have higher PMPM expenditure than non-diabetic patients. The difference between PMPM expenditure in non-diabetic and diabetic patients becomes less pronounced with increasing age.

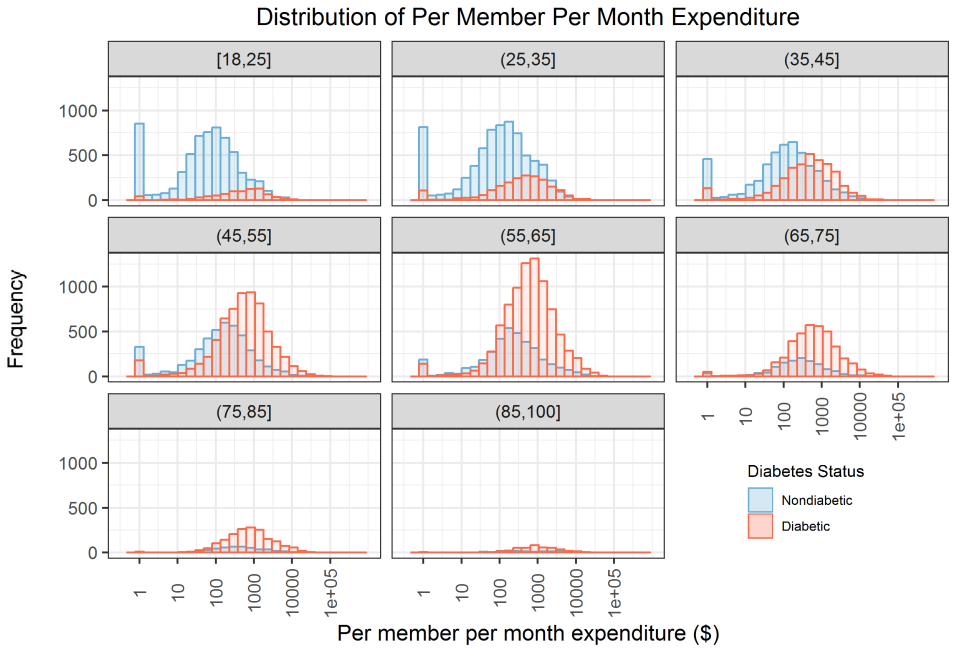

Figure 3.5: Frequency of Per Member Per Month Expenditures by Age Category

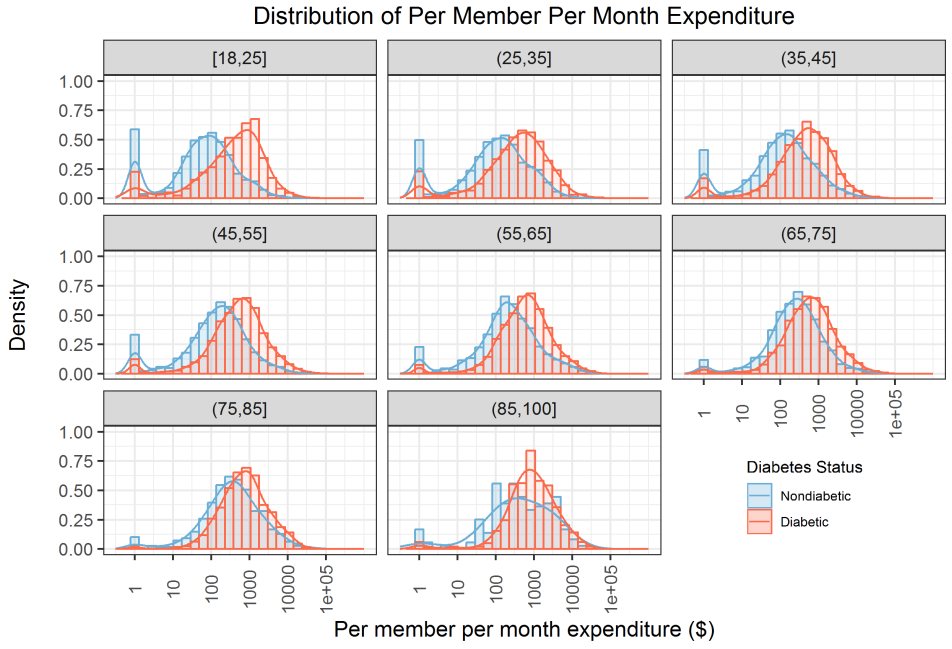

Figure 3.6: Density of Per Member Per Month Expenditures by Age Category

There are more members with near-zero PMPM expenditure in the younger age strata, especially in the non-diabetic population (Figure 3.6). These low PMPM expenditures are driven by patients with a high proportion of months with no expenditure. Across the population, 31.2% of monthly expenditure records are zero. 36,147 patients out of 56,349 have at least one month in which they have no medical expenditure. 19,810 (55%) of these are between 18 and 45 years old.

If we further stratify diabetes status to include non-diabetic, pre-diabetic, and diabetic populations, we see the pre-diabetic patients have a more diffuse distribution that falls approximately between that of the non-diabetics and diabetics (Figure 3.7).

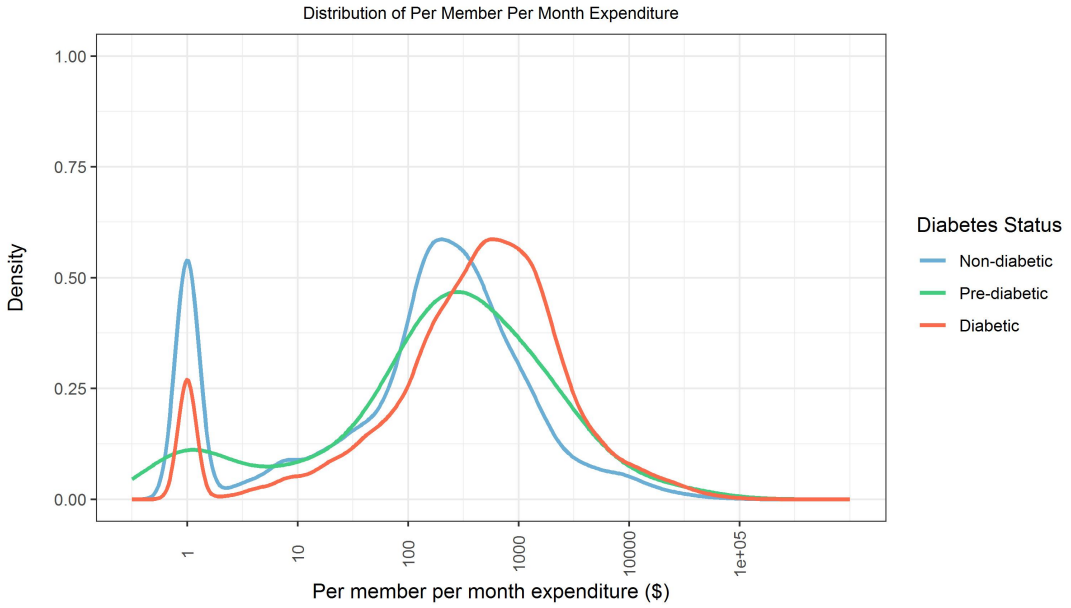

Figure 3.7: Density of Per Member Per Month Expenditure by Diabetes Diagnosis

3.4 Population Disenrollment

We group disenrollment into three categories: (1) disenrollment due to death, (2) disenrollment due to changing plan, and (3) disenrollment for other reasons. There are a total of 322 deaths (0.6% of population), 304 plan changes (0.5% of population), and 9,917 disenrollments for other reasons (18% of population). Counts of deaths, plan changes, and disenrollments for other reasons are stratified by RUB score and diabetes status in Table 3.4, Table 3.5, and Table 3.6.

Table 3.4: Non-diabetic and diabetic member deaths by RUB Score

RUB Score	**Non-diabetic Members** N (%)	**Diabetic Members** N (%)	**Total** N (%)
1	5 (1.6)	2 (0.6)	7 (2.2)
2	6 (1.9)	0 (0.0)	6 (1.9)
3	16 (5.0)	6 (1.9)	22 (6.9)
4	18 (5.6)	22 (6.8)	40 (12.4)
5	84 (26.1)	163 (50.6)	247 (76.7)
Total	129 (40.1)	193 (59.9)	322 (100)

Table 3.5: Non-diabetic and diabetic member plan changes by RUB Score

RUB Score	**Non-diabetic Members** N (%)	**Diabetic Members** N (%)	**Total** N (%)
1	53 (17.4)	0 (0.0)	53 (17.4)
2	34 (11.2)	0 (0.0)	34 (11.2)
3	132 (43.4)	2 (0.7)	134 (44.1)
4	51 (16.8)	3 (1.0)	54 (17.8)
5	23 (7.5)	6 (2.0)	29 (9.5)
Total	293 (96.4)	11 (3.6)	304 (100)

Table 3.6: Non-diabetic and diabetic member disenrollments due to other reasons by RUB Score

RUB Score	**Non-diabetic Members** N (%)	**Diabetic Members** N (%)	**Total** N (%)
1	1271 (12.8)	47 (0.5)	1318 (13.3)
2	1351 (13.6)	39 (0.4)	1390 (14.0)
3	3776 (38.1)	516 (5.2)	4292 (43.3)
4	1694 (17.1)	491 (5.0)	2185 (22.0)
5	388 (3.9)	344 (3.5)	732 (7.4)
Total	8480 (85.5)	1437 (14.5)	9917 (100)

Chapter 4

Methods for Prediction of Intervention Effects (PIE)

We use administrative, claims, and clinical data from JHHC to model member enrollment, health state, medical expenditure, and disenrollment. We use these models to develop a simulation-based approach to predicting intervention effects and their uncertainties.

4.1 Observed System Hierarchical Models

4.1.1 Enrollment

We explore enrollment by looking for spatial patterns in the state of Maryland. Spatial patterns of interest include (1) which regions have the most diabetic enrollees and (2) which regions have the highest proportion of diabetic enrollees. We model the observed counts using Poisson regression and the observed proportions using binomial regression as a smooth function of the centroids of each ZIP code. We then visually assess the estimated distributions.

4.1.2 Health State Given Enrollment

We use Resource Utilization Band (RUB) score as a proxy for health state. As discussed in section 3.2, an individual with a RUB score of 1 is a low utilizer and an individual with a RUB score of 5 is a high utilizer, with 2, 3, and 4, as intermediate and ordered levels of utilization. Note that RUB score is categorical; however, we model RUB score as if following a Gaussian distribution. Specifically, we model RUB score as a linear function of diabetes status, sex, a smooth function of age, and a smooth function of month with random intercepts and slopes at the individual level. We allow the effect of diabetes to differ by sex and age.

4.1.3 Expenditure Given Enrollment and Health State

As discussed in section 3.3, 31.2% of monthly expenditure records are zero. Due to the high proportion of zeros, we model the probability of having a positive expenditure and the size of the positive expenditure as separate processes. We model the log odds of having a positive expenditure as a linear function of RUB score, diabetes status, sex, a smooth function of age, and a smooth function of month with random intercepts at the individual level. Due to the positive skew of medical expenditure data, we model log expenditure as a linear function of RUB score, diabetes status, sex, a smooth function of age, and a smooth function of month with random intercepts and slopes at the individual level. We allow the effect of diabetes to differ by sex, age, and RUB score. We allow the effect of age to differ by RUB score.

We are ultimately interested in making predictions and inference on the untransformed scale (i.e. dollars rather than log dollars), so we calculate the smearing estimate $\frac{1}{n}\sum_{i=1}^{n}\exp\{\boldsymbol{x}_0\hat{\beta}+\hat{\varepsilon}_i\}$ where $\boldsymbol{x}_0$ is the design matrix, $\hat{\beta}$ are the least squares estimates, and $\hat{\varepsilon}_i$ are the least squares residuals (Duan, 1983). The smearing estimate can be decomposed into the regression effect $\exp\{\boldsymbol{x}_0\hat{\beta}\}$ and the skewness effect or smearing coefficient $\frac{1}{n}\sum_{i=1}^{n}\exp\{\hat{\varepsilon}_i\}$. To allow for heterogeneity in the relationship between the covariates and smearing coefficient, we regress the exponeniated residuals on the same predictors as were used in the original log-linear model. The predictions from this model estimate the smearing coefficient for any combination of covariates.

4.1.4 Disenrollment Given Enrollment and Health State

We model disenrollment using a discrete-time hazard model, formulated as three Poisson regression models: (1) disenrollment due to death in the current month, (2) disenrollment due to changing plan given survival in the current month, and (3) disenrollment for other reasons given survival and not changing plan in the current month. We model disenrollment as a function of RUB score, diabetes status, sex, a smooth function of age, and a smooth function of month.

Component	Conditioned on:	Outcome	Model
Enrollment			
	—	Proportion diabetic	Binomial GLM
	—	Number diabetic	Poisson GLM
Health State	Enrollment	RUB score	Linear mixed model
Expenditure			
• Probability	Enrollment Health State	Probability of positive expenditure	Binomial GLMM
• Size	Enrollment Health State Positive Expenditure	Size of positive expenditure	Log-linear mixed model
Disenrollment			
• Death	Enrollment Health State	Hazard of death	Discrete-time hazard model
• Change plan	Enrollment Health State Survival	Hazard of changing plan	Discrete-time hazard model
• Other	Enrollment Health State Survival Not changing plan	Hazard of disenrollment for other reasons	Discrete-time hazard model

4.2 Simulation

4.2.1 Enrollment

We draw a random sample with replacement from the observed population. Individuals are drawn with their respective covariates (i.e. age, sex, diabetes status). Individuals are detached from the outcomes of interest (i.e. monthly RUB score and expenditure). We expand the number of records associated with each individual to include all months starting at the observed month of enrollment up to month 12. For example, if an individual enrolled in the observed population at month 3 and disenrolled at month 6, we enroll a person with the same characteristic set of covariates at month 3 and retain them in the population until either month 12 or the month in which any of the disenrollment models predict their departure, whichever happens sooner.

4.2.2 Health state

We use the model-based distributions of fixed and random effects to simulate health states in the following manner:

1. Obtain the fixed effects design matrix and call this $\boldsymbol{X}$. This design matrix contains columns corresponding to each of the covariates in the health state model. $\boldsymbol{X}$ is a block matrix of N vertically stacked blocks, where N is the number of individuals in the simulated population. The covariates corresponding to individual i populate block i. The number of rows in each block is determined by the month in which the corresponding individual enrolled in JHHC; each block will have one row per month from the month of enrollment through month 12.

2. Obtain the random effects design matrix and call this $\boldsymbol{Z}$. This design matrix has a column of ones for the random intercepts and a column of month numbers for the random slopes. As above, this will be a block matrix composed of N vertically stacked blocks, where N is the number of enrolled individuals in the simulated population. To illustrate, consider two individuals i and j: if individual i enrolls in month 1, then block i of the random effects design matrix will be a 12×2 matrix with a column of ones and a column containing the values 1 through 12. If individual j enrolls in month 3, block j of the random effects design matrix will be a 10×2 matrix with a column of ones and a column containing the values 3 through 12. The remaining blocks will be filled similarly.

3. Obtain a random sample from the model-based distribution of fixed effects and call this β_{sim}. The model-based distribution is multivariate Gaussian with mean equal to the fixed effects coefficients $\hat{\beta}$ and variance-covariance matrix equal to the fixed effects variance-covariance matrix $\hat{\boldsymbol{V}}$.

$$\beta_{\text{sim}} \sim MVG\left(\hat{\beta}, \hat{\boldsymbol{V}}\right)$$

4. For each individual i, obtain a random sample from the model-based distribution of random effects and call this $b_{\text{sim},i}$; $b_{\text{sim},i}$ will be a 2×1 vector with a random intercept and a random slope. The model-based distribution is multivariate Gaussian with mean $\mathbf{0}$ and variance-covariance matrix equal to the random effects variance-covariance matrix $\hat{\boldsymbol{D}}$.

$$b_{\text{sim},i} \sim MVG\left(\mathbf{0}, \hat{\boldsymbol{D}}\right)$$

5. Obtain error terms ε_{sim} for each record. These will be drawn from a Gaussian with mean 0 and variance $\hat{\sigma}^2$, where $\hat{\sigma}^2$ is the estimated population variance.

$$\varepsilon_{\text{sim}} \sim G\left(0, \hat{\sigma}^2\right)$$

6. Calculate the simulated health states for each individual where $[\boldsymbol{X}]_i$ refers to block i of the fixed effects design matrix and $[\boldsymbol{Z}]_i$ refers to block i of the random effects design matrix:

$$\text{RUB}_i = [\boldsymbol{X}]_i \beta_{\text{sim}} + [\boldsymbol{Z}]_i b_{\text{sim},i} + \varepsilon_{\text{sim},i}$$

7. Round the simulated RUB score to the nearest integer. If the nearest integer is less than 1, set the RUB score equal to 1. If the nearest integer is greater than 5, set the RUB score equal to 5.

4.2.3 Expenditure

4.2.3.1 Probability of Positive Expenditure

We expand the fixed effects design matrix from the health state simulation to include a column for the simulation-based RUB score. We then use the model-based distributions of fixed and random effects to simulate the probability of positive expenditure in the same manner as that described in steps 3-6 above (subsection 4.2.2).

Our simulated responses are log odds of positive expenditure in each month. We transform these to be on the probability scale. To simulate whether the expenditure *is* positive, we sample from a binomial distribution with

probability of success equal to the simulated probability. For example, suppose we obtain probability p_{ij} for individual i in month j. To simulate whether individual i will have a positive expenditure in month j, we sample from a binomial distribution with probability of success p_{ij}. If this yields a success, then individual i has a positive expenditure in month j. If this yields a failure, then individual i has no expenditure in month j.

4.2.3.2 Size of Positive Expenditure

We expand the fixed effects design matrix from the expenditure probability simulation to include columns for the interaction between RUB score and age, sex, and diabetes status. We then use the model-based distributions of fixed and random effects to simulate the size of the medical expenditure in the same manner as described in steps 3-6 above (subsection 4.2.2). Our simulated responses are log dollars so we exponentiate to obtain dollars.

4.2.4 Disenrollment

We obtain the simulated probabilities of death, changing plan given survival, and leaving for other reasons given survival and not changing plan in the following abbreviated version of the procedure described in subsection 4.2.2:

1. Obtain the fixed effects design matrix $\boldsymbol{X}$ (n.b. the fixed effects design matrix for our Poisson models is entirely contained within the fixed effects design matrix for our log-linear model so can be easily obtained by selecting the relevant columns).

2. Obtain a random sample from the model-based distribution of fixed effects for each Poisson model. The model-based distribution is multivariate Gaussian with mean equal to the fixed effects coefficients $\hat{\beta}$ and variance-covariance matrix equal to the fixed effects covariance matrix $\hat{\boldsymbol{V}}$.

$$\beta_{\text{sim, death}} \sim MVG\left(\hat{\beta}_{\text{death}}, \hat{\boldsymbol{V}}_{\text{death}}\right)$$
$$\beta_{\text{sim, change}} \sim MVG\left(\hat{\beta}_{\text{change}}, \hat{\boldsymbol{V}}_{\text{change}}\right)$$
$$\beta_{\text{sim, other}} \sim MVG\left(\hat{\beta}_{\text{other}}, \hat{\boldsymbol{V}}_{\text{other}}\right)$$

3. Calculate the simulated probability for each event. Let $p_{\text{death},ij}$ denote the probability of death for individual i in month j, $p_{\text{change},ij}$ denote the probability of changing plan given survival for individual i in month j, and $p_{\text{other},ij}$ denote the probability of leaving for other reasons given survival and not changing plan for individual i in month j. Let $[\boldsymbol{X}]_i$ denote block i of the fixed effects design matrix.

$$p_{\text{death},ij} = \exp\left\{[\boldsymbol{X}]_i \beta_{\text{sim, death}}\right\}$$
$$p_{\text{change},ij} = \exp\left\{[\boldsymbol{X}]_i \beta_{\text{sim, change}}\right\}$$
$$p_{\text{other},ij} = \exp\left\{[\boldsymbol{X}]_i \beta_{\text{sim, other}}\right\}$$

4. Predict whether individual i will disenroll in month j by sampling from a binomial distribution with probability of success equal to $p_{\text{death},ij}$, $p_{\text{change},ij}$, and $p_{\text{other},ij}$ in turn. If any of the three trials yields a success, we predict individual i disenrolls in month j.

5. Remove all records subsequent to an individual's predicted disenrollment.

4.3 Prediction of Intervention Effects

We propose the causal pathway shown in Figure 4.1. Each node corresponds to one of the component models from section 4.1. This framework forms the basis for our simulation-based approach to predicting intervention effects.

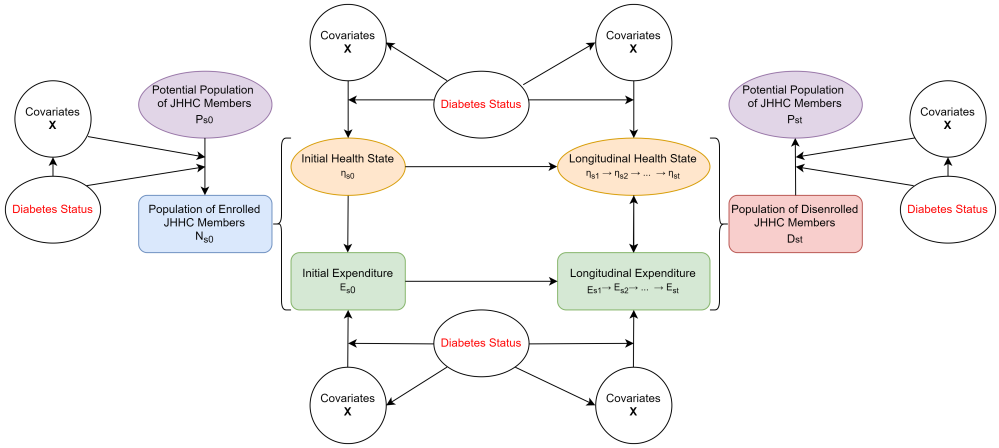

Figure 4.1: Eligible members enroll in JHHC and are assigned an initial health state. Members have an initial expenditure which is influenced by this initial health state. Longitudinal health state depends on previous health states and longitudinal expenditure depends on concurrent health state and previous expenditures. Members can disenroll in any month as influenced by their health state and expenditure. Enrollment, health state, expenditure, and disenrollment can each be influenced by diabetes status and other demographic data such as sex and age.

To demonstrate, we simulate two interventions using our prediction of intervention effects (PIE) model. The first intervention is to decrease the effect of diabetes by 0-5% in the health state and expenditure models. The second is to reduce patients' plasma glucose concentration (HbA1c) by 0-1%.[1] These two interventions illustrate the flexibility of our approach because the health state model takes a different form in each but the overarching structure of the PIE model remains unchanged.

[1] 0-1% is an absolute (i.e. not percent) reduction in HbA1c. HbA1c is reported as a percent.

4.3.1 Intervention 1: Reduce Diabetes Effect

We follow the same simulation procedure as defined above with small modifications to the health state and expenditure models. Specifically, we take the simulated diabetes coefficient from each model and iteratively multiply it by a value α_i between 0.95 and 1 (Equation 4.1).

$$\beta_{\text{sim}} = \begin{bmatrix} \beta_0 \\ \vdots \\ \beta_{\text{Diabetes}} \\ \vdots \\ \beta_p \end{bmatrix} \longrightarrow \begin{bmatrix} \beta_0 \\ \vdots \\ \alpha_i \times \beta_{\text{Diabetes}} \\ \vdots \\ \beta_p \end{bmatrix} = \beta^*_{\text{sim}} \tag{4.1}$$

In each iteration, we multiply the diabetes coefficient in the health state model by α_1 and the diabetes coefficient in the expenditure models by α_2. We sample (α_1, α_2) from a grid of the plane $[0.95, 1] \times [0.95, 1]$ such that we obtain good coverage of the possible combinations of modifications to the health state and expenditure models.[2] All other coefficients remain the same throughout the iterations.

The remainder of the simulation procedure proceeds exactly as above but with β^*_{sim} rather than β_{sim}. We calculate (1) the improvement in mean RUB score, (2) per member per month savings, and (3) annual savings for every combination of (α_1, α_2).

[2] We have been using a 15×15 grid for a total of 225 combinations.

4.3.2 Intervention 2: Reduce Average Plasma Glucose

We assume a causal relationship between HbA1c and medical expenditure (Lissovoy, Ganoczy, and Ray, 2000). We subset the population to include only those who are in Medicare Advantage and have HbA1c data, thereby obtaining 661 members and 999 member months. We replace the RUB score model with a model for plasma glucose concentration. We follow the same simulation procedure as above but in evaluating the counterfactual, we subtract 0-1 from predicted HbA1c values (i.e. we modify one column of the design matrix). We calculate the per member per month savings under intervention conditions.

Chapter 5

Results

5.1 Hierarchical models

5.1.1 Enrollment

Between July 2017 and June 2018, there were 28,489 diabetic and 467,274 non-diabetic JHHC members. Thus, approximately 6.1% of JHHC members were *known* diabetics during this time frame. This is somewhat lower than the national average of 7.1% (CDC, 2017b).[1] Our model of the proportion of diabetics by Maryland ZIP code estimates higher proportions of diabetic members in the southern end of the Eastern Shore, Washington County, and east and west Baltimore (Figure 5.1).

The regions with the highest proportion of diabetics roughly correspond to the regions with the largest absolute number of enrolled diabetics. Our model of the number of diabetics by Maryland ZIP code estimates the highest number of diabetic enrollees in the southern end of the Eastern Shore, and east and west Baltimore. Washington County is estimated to have a high proportion of diabetics but not a large absolute number of enrollees (Figure 5.2).

[1] The CDC estimates a national average of 9.4% but 23.8% of these cases are undiagnosed.

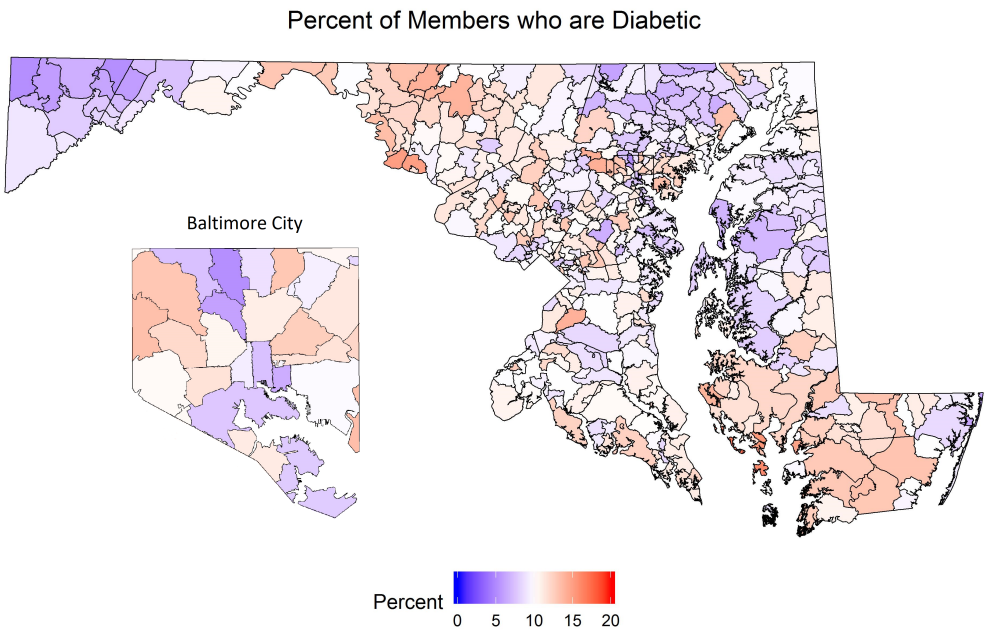

Figure 5.1: Smoothed percent of members who are diabetic by ZIP code

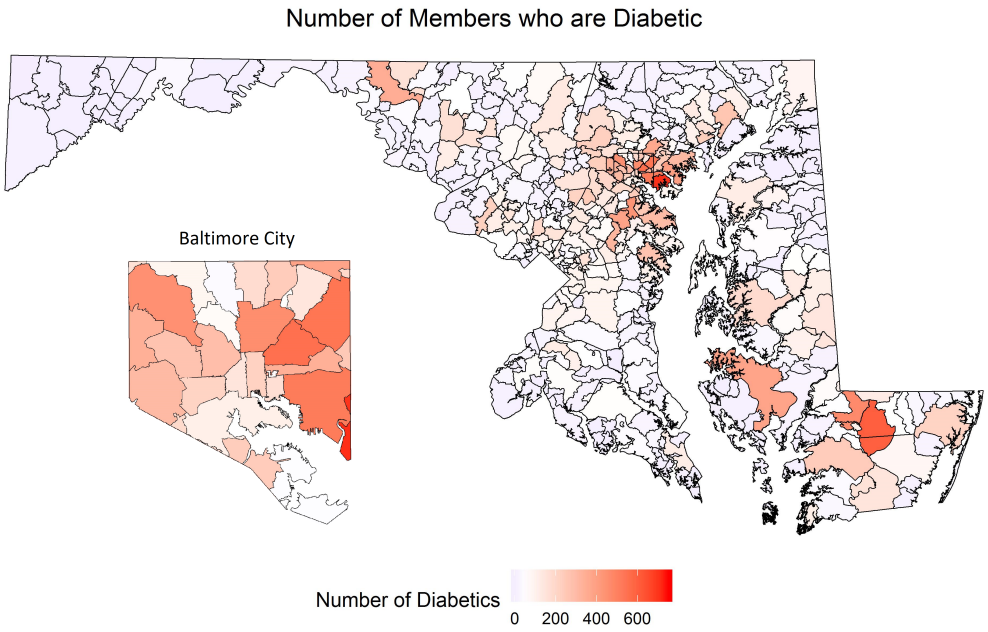

Figure 5.2: Smoothed number of diabetic members by ZIP code

5.1.2 Health State

Recall that we use RUB score as a proxy for health state, with high RUB scores indicating higher medical resource utilization than low RUB scores. Further, recall that we model RUB score as continuous despite it being discrete. In our model, we control for diabetes status, age, sex, and month.

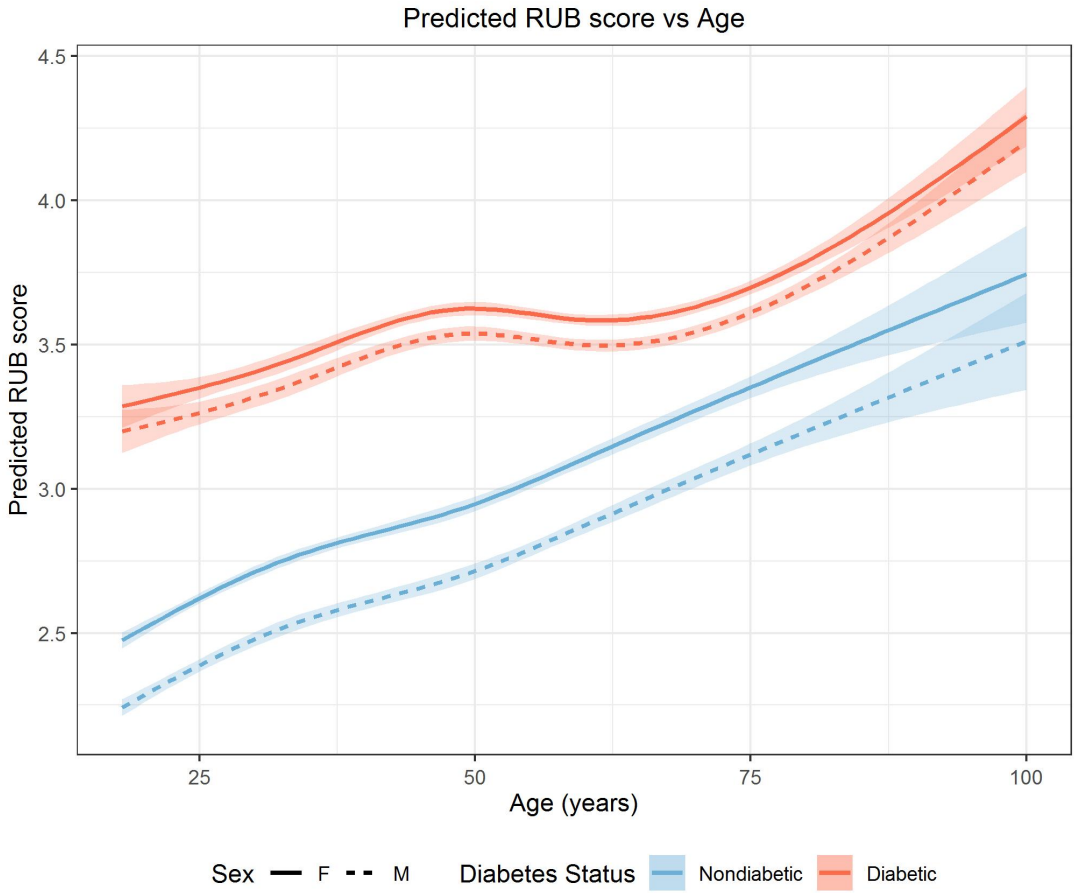

Figure 5.3: Predicted RUB score for patients in January 2018 with 95% confidence bands. The relationship between age and RUB score is the same in other months; January 2018 was chosen for convenience.

We estimate that a female diabetic patient will have a RUB score $0.82_{(0.044)}$ units higher than an otherwise similar non-diabetic patient. We estimate that a male diabetic patient will have a RUB score $0.97_{(.045)}$ units higher than an otherwise similar non-diabetic patient. Though the estimated effect of diabetes on health state is greater in male than female patients, non-diabetic male patients have a RUB score $0.23_{(0.011)}$ units lower than otherwise similar non-diabetic female patients (Table 5.1). The result of males having a lower baseline RUB score but higher estimated diabetes effect is that male and female diabetics have very similar RUB scores to each other. Male diabetics still have lower RUB scores than otherwise similar females but by less of a margin than when comparing non-diabetic males and females. There is a strong positive association between RUB score and age (i.e. worsening health state with increasing age). Between 50-70 years of age, the separation between diabetics and non-diabetics becomes less pronounced (Figure 5.3).

Table 5.1: RUB Score model results

Coefficient	$\hat{\beta}^*$	$\widehat{\text{SE}}\left(\hat{\beta}\right)$	t value
Female	2.315	0.017	140.25
Male	2.082	0.017	124.6
Diabetes			
• Female	0.824	0.044	18.53
• Male	0.970	0.045	21.64

* $\hat{\beta}$ corresponds to the mean effect for each subgroup.

5.1.3 Expenditure

5.1.3.1 Probability of Positive Expenditure

We estimate that the odds of a diabetic patient having positive expenditure are 4.3 times that of an otherwise similar non-diabetic patient and that the odds of a male patient having positive expenditure are 0.61 that of an otherwise similar female patient (Table 5.2).

Table 5.2: Probability of positive expenditure model results

Coefficient	$\hat{\beta}^*$	$\hat{\text{SE}}(\hat{\beta})$	z value
RUB 1 (ref)	-1.174	0.035	-33.57
RUB 2	0.569	0.022	26.23
RUB 3	1.258	0.019	64.86
RUB 4	1.851	0.023	80.87
RUB 5	2.759	0.032	85.76
Diabetes	1.451	0.019	75.66
Male	-0.486	0.017	-27.97

* $\hat{\beta}$ for the reference group corresponds to the log odds of positive expenditure. $\hat{\beta}$ for all other groups corresponds to the log of the odds ratio between that group and the reference group.

In Figure 5.4, we transform to the probability scale and explore the relationship between RUB score and positive expenditure stratified by diabetes diagnosis. A diabetic patient with RUB score 1 has a similar probability of positive expenditure to an otherwise similar non-diabetic with RUB score 3. This suggests that the effect of diabetes on positive expenditure goes above and beyond that explained by RUB score. Specifically, the probability of expenditure for a diabetic patient is like that of otherwise similar non-diabetic patient with a RUB score that is two units higher. We see this pattern for diabetics with RUB scores 1, 2, and 3.

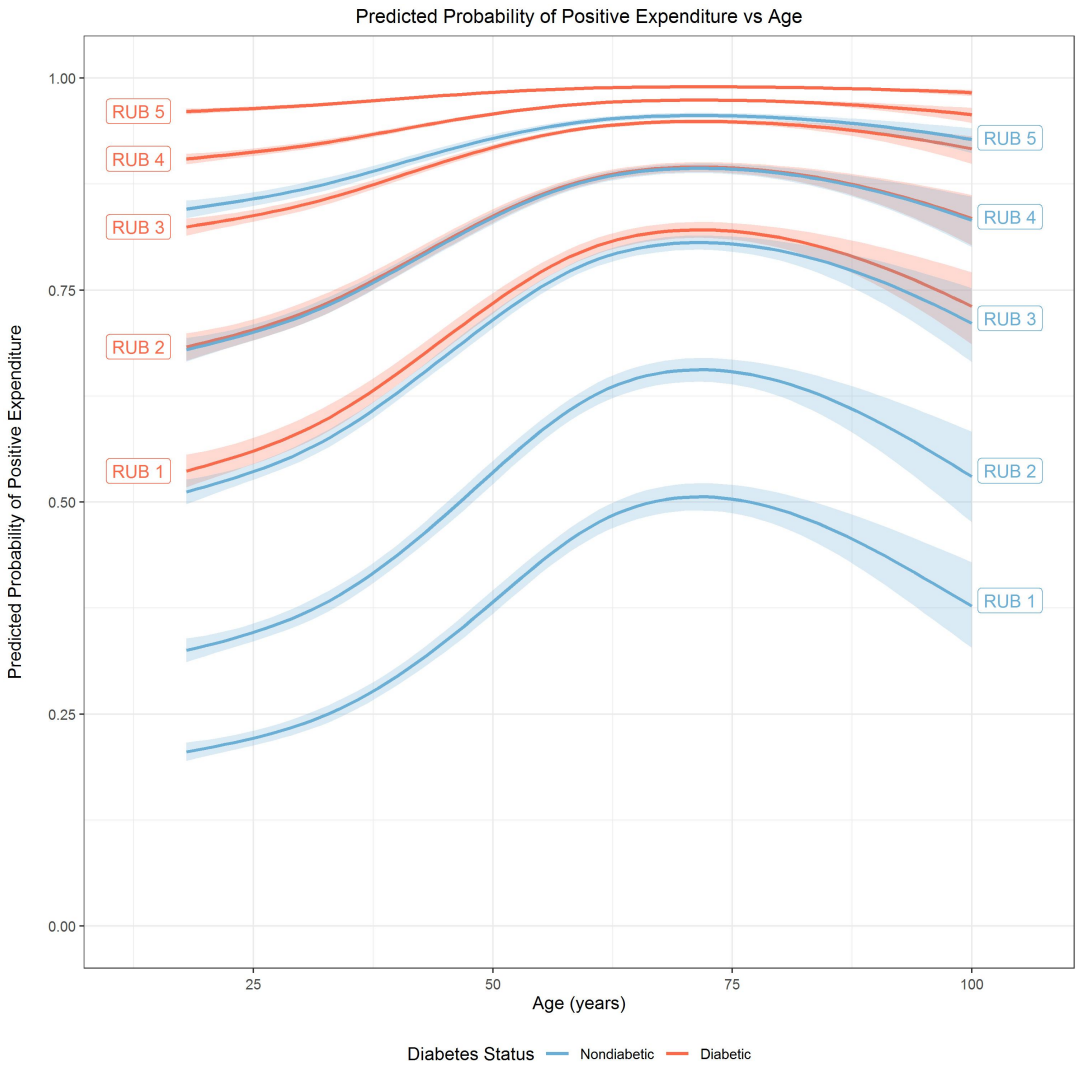

Figure 5.4: Predicted probability of positive expenditure with 95% confidence bands.

5.1.3.2 Size of Positive Expenditure

We estimate that a diabetic patient's monthly expenditure is approximately 2.3 times that of an otherwise similar non-diabetic patient's. There is no compelling evidence that the effect of diabetes differs between men and women (Table 5.3).

Estimated expenditure increases with increasing RUB score. A non-diabetic patient with RUB score 2, 3, 4, or 5 spends 1.74, 2.57, 4.37, or 7.86 times that of an otherwise similar patient with RUB score 1, respectively. The estimated effect of increasing RUB score is somewhat lower in diabetic patients than non-diabetic patients in all but RUB score 5. A diabetic patient with RUB score 2, 3, 4, or 5 spends 1.43, 2.33, 4.12, or 7.93 that of an otherwise similar patient with RUB score 1, respectively.

Table 5.3: Size of positive expenditure model results

Coefficient	$\hat{\beta}^*$	$\hat{\text{SE}}(\hat{\beta})$	z value
RUB 1 (ref)	4.214	0.028	151.81
RUB 2	0.556	0.022	25.634
RUB 3	0.944	0.019	49.73
RUB 4	1.474	0.021	69.10
RUB 5	2.062	0.0282	73.80
Male	0.016	0.015	1.08
Diabetes	0.835	0.062	13.41
Diabetes : Male	-0.031	0.020	-1.55
Diabetes : RUB 2	-0.198	0.039	-5.02
Diabetes : RUB 3	-0.096	0.033	-2.93
Diabetes : RUB 4	-0.058	0.035	-1.66
Diabetes : RUB 5	0.009	0.040	0.24

* $\hat{\beta}$ for the reference group corresponds to the expected geometric mean of log expenditure for non-diabetic female patients with RUB score 1. $\hat{\beta}$ for all other groups corresponds to the difference in the expected geometric mean of log expenditure between that group and the reference group.

To obtain meaningful predicted expenditures, we exponentiate predicted log dollars and multiply by the smearing coefficient. Smearing coefficient model results can be found in the the Appendix (chapter 7).

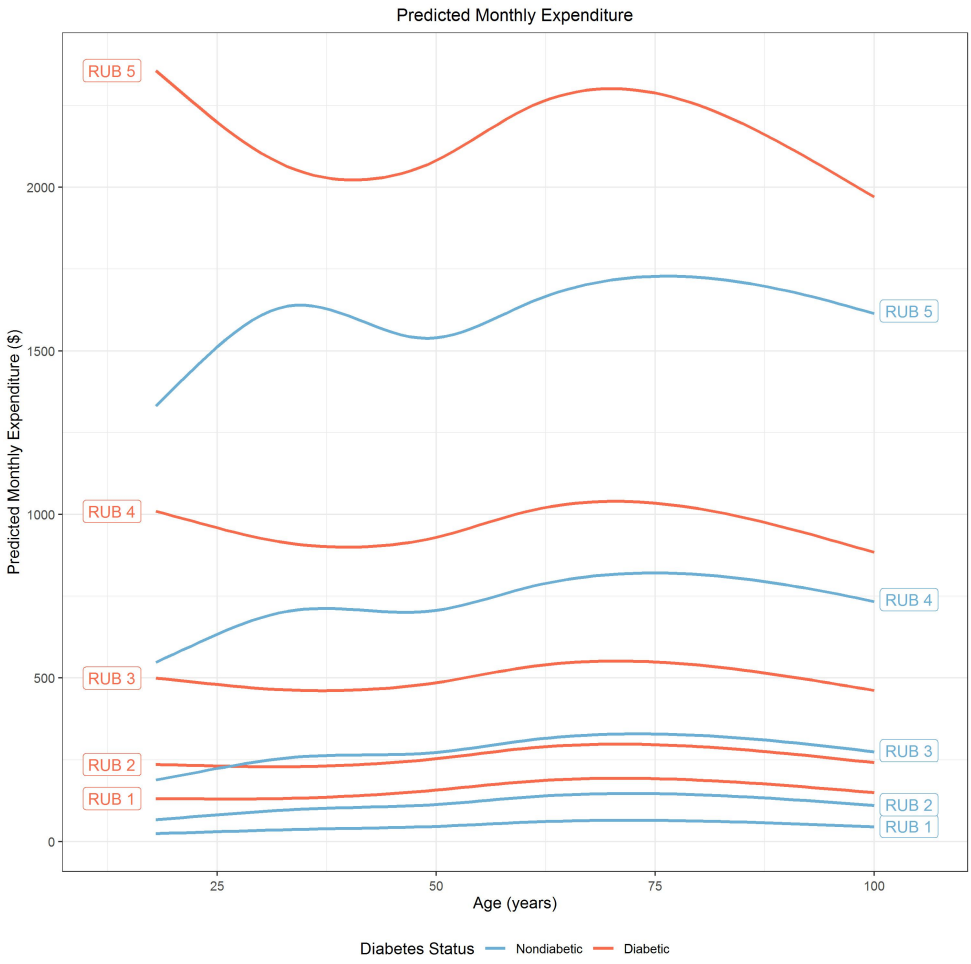

Figure 5.5: Predicted size of positive expenditure after transforming from log dollars to dollars and multiplying by the smearing coefficient.

In Figure 5.5 we see that diabetics with a positive expenditure have a higher monthly average than otherwise similar non-diabetics with a positive expenditure and that monthly expenditure tends to increase with increasing RUB score. The predicted expenditures are largely unrelated to increasing age after stratifying by diabetes diagnosis and RUB score. This pattern is surprising and was further explored to confirm it is a feature of the observed data (see chapter 7).

5.1.4 Disenrollment

We explore disenrollment in three successive discrete-time hazards models implemented using Poisson regression. The first explores the hazard of death. We find that the hazard of death is approximately 50% lower in diabetics than otherwise similar non-diabetics (Table 5.4). Given the same same age, gender, diabetes status, and health state, the hazard of death is similar among patients with RUB scores 1, 2, and 3. It is approximately 1.76 times higher for patients with RUB score 4 than otherwise similar patients with RUB score 1, and 29.49 times higher for patients with RUB score 5 than otherwise similar patients with RUB score 1 (Figure 5.6).

The second model explores the hazard of disenrollment due to changing plan given survival. We find that the conditional hazard is approximately 97% lower in diabetics than otherwise similar non-diabetics (Table 5.5). All else equal, the conditional hazard of disenrollment due to changing plan is similar across RUB scores, similar between male and female patients, and increases with increasing age in non-diabetic patients (Figure 5.7).

The third model explores the hazard of disenrollment due to other reasons given survival and not changing plan. We find that the conditional hazard is approximately 75% lower in diabetics than otherwise similar non-diabetics (Table 5.6). The conditional hazard is lowest in RUB scores 1, 2, and 3, and decreases with increasing age (Figure 5.8).

A common theme in all three models is that diabetic patients have lower hazard of disenrollment than non-diabetic patients. The effect of this phenomenon is a long-term increase in the fraction of diabetics relative to their respective rate of enrollment.

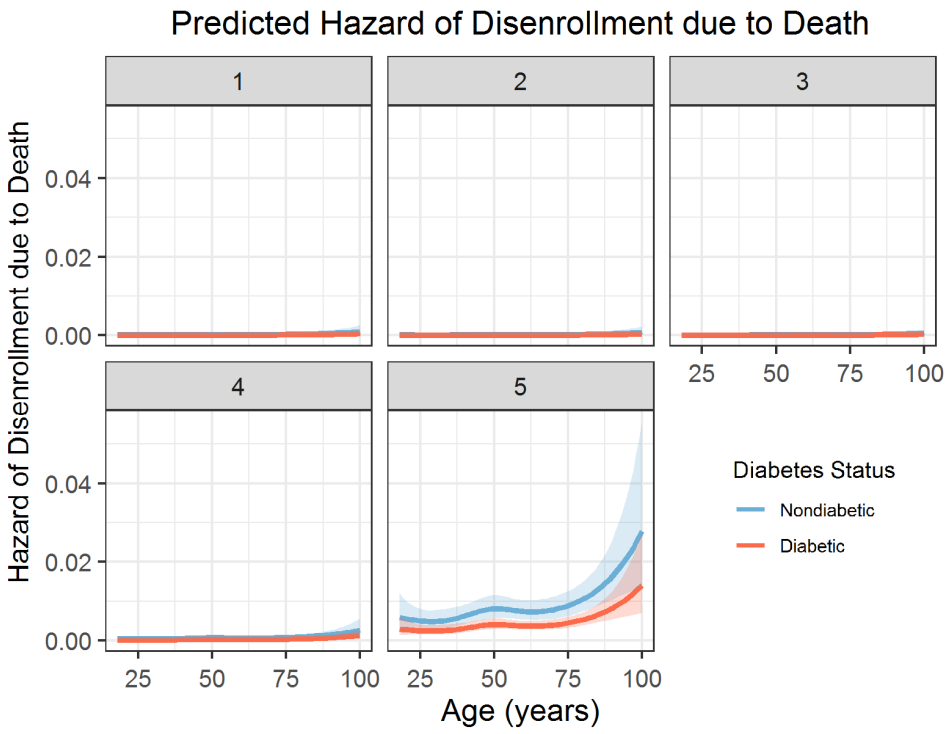

Figure 5.6: Each panel shows the hazard of disenrollment due to death for a male patient in January 2018. The five panels correspond to the five RUB scores, as indicated by the banner over each plot.

Table 5.4: Disenrollment due to death

Coefficient	$\hat{\beta}^*$	$\widehat{\text{SE}}(\hat{\beta})$	z value
RUB 1 (ref)	-9.243	0.520	-17.79
RUB 2	-0.198	0.556	-0.356
RUB 3	-0.387	0.437	-0.885
RUB 4	1.017	0.417	2.44
RUB 5	3.384	0.398	8.50
Diabetes	-0.683	0.122	-5.59
Male	0.379	0.113	3.35

* $\hat{\beta}$ for the reference group corresponds to the log hazard of disenrollment due to death. $\hat{\beta}$ for all other groups corresponds to the difference in log hazard between that group and the reference group.

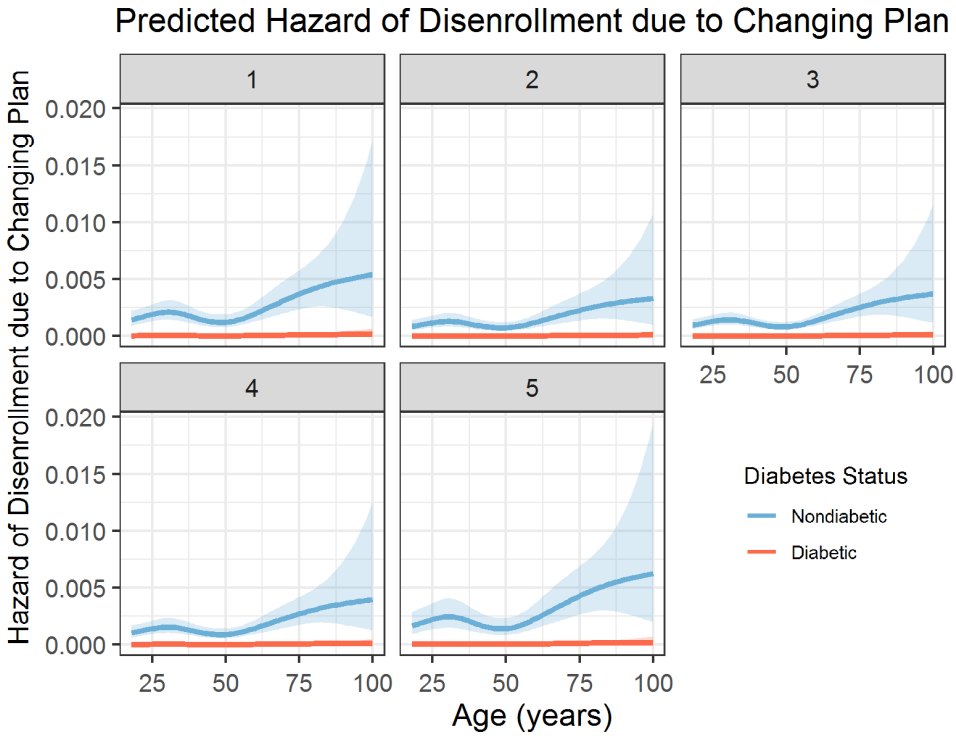

Figure 5.7: Each panel shows the hazard of disenrollment due to changing plan given survival for a male patient in January 2018. The five panels correspond to the five RUB scores, as indicated by the banner over each plot.

Table 5.5: Disenrollment due to changing plan given survival

Coefficient	$\hat{\beta}^*$	$\widehat{\text{SE}}(\hat{\beta})$	z value
RUB 1 (ref)	-6.849	0.278	-24.64
RUB 2	-0.488	0.220	-2.22
RUB 3	-0.376	0.165	-2.29
RUB 4	-0.311	0.197	-1.58
RUB 5	0.145	0.243	0.60
Diabetes	-3.404	0.315	-10.82
Male	-0.197	0.124	-1.59

* $\hat{\beta}$ for the reference group corresponds to the log hazard of disenrollment due to changing plan given survival. $\hat{\beta}$ for all other groups corresponds to the difference in log hazard between that group and the reference group.

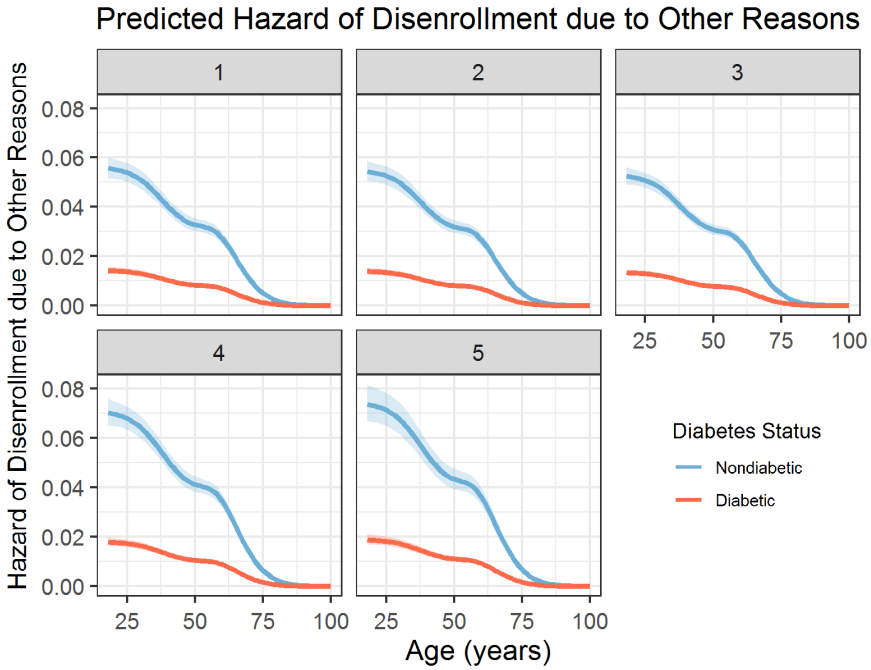

Figure 5.8: Each panel shows the hazard of disenrollment for other reasons given survival and not changing plan for a male patient in January 2018. The five panels correspond to the five RUB scores, as indicated by the banner over each plot.

Table 5.6: Disenrollment due to other reasons given survival and not changing plan

Coefficient	$\hat{\beta}^*$	$\widehat{\text{SE}}\left(\hat{\beta}\right)$	z value
RUB 1 (ref)	-3.456	0.500	-69.21
RUB 2	-0.024	0.038	-0.62
RUB 3	-0.059	0.032	-1.85
RUB 4	0.233	0.036	6.47
RUB 5	0.282	0.049	5.80
Diabetes	-1.366	0.031	-43.57
Male	-0.108	0.022	-4.96

* $\hat{\beta}$ for the reference group corresponds to the log hazard of disenrolling for other reasons given survival and not changing plan. $\hat{\beta}$ for all other groups corresponds to the difference in log hazard between that group and the reference group.

5.2 Simulations

5.2.1 Health State

Our health state simulation does not resemble the observed health state distribution as closely as we would like it to. However, the simulated health state distributions mimic many important features of the initial population. Specifically, we see there tend to be fewer diabetics with RUB score 1 or 2 than non-diabetics across all age strata. Both diabetics and non-diabetics have high proportions of patients with RUB score 3 across age strata. The proportion of diabetic patients with RUB score 4 or 5 surpasses that of the non-diabetics. These are all patterns we noted in the observed population (section 3.2).

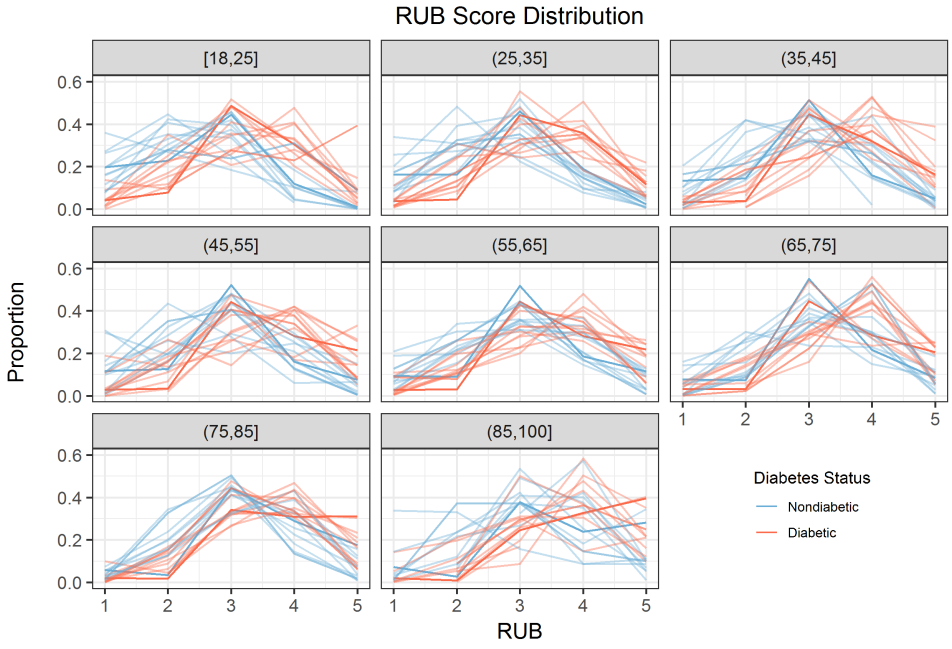

Figure 5.9: Each panel corresponds to one of eight age strata, as indicated by the age interval in each banner. Each panel shows the simulated health state distribution from 10 simulations. The bold line shows the observed health state distribution.

5.2.2 Expenditure

Recall that our simulated PMPM expenditure is the product of three models: probability of positive expenditure, size of positive expenditure, and smearing coefficient. Our simulated PMPM expenditure distributions closely resemble the observed expenditure distribution (Figure 5.10). One of the lines in each panel corresponds to the observed PMPM expenditure distribution; the simulated PMPM expenditure distributions mimic reality closely enough that the observed distribution is indistinguishable from the simulated distributions. PMPM expenditure is higher in diabetic patients than non-diabetic patients and the margin separating the distributions diminishes with increasing age. Our simulations appear to capture these important features of the observed PMPM expenditure distribution.

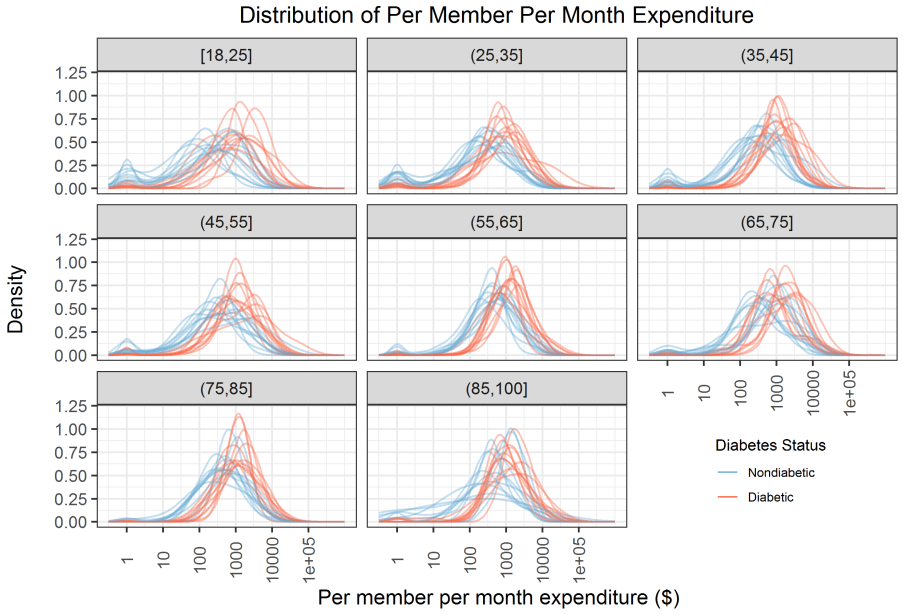

Figure 5.10: Each panel corresponds to one of eight age strata, as indicated by the age interval in each banner. Each panel shows the simulated PMPM expenditure distribution from 10 simulations. One of the 11 lines shows the observed PMPM expenditure distribution.

5.2.3 Disenrollment

Our models for disenrollment due to death and changing plan perform well in the simulations. Our model for disenrollment due to other reasons overestimates the number of disenrollments by approximately 10%. In the observed population, there are 322 deaths (0.6% of the population), 304 plan changes (0.5% of the population), and 9,917 disenrollments for other reasons (18% of the population). In 100 simulations, we predict an average of 311.8 deaths, 332.6 plan changes, and 1,1067.5 disenrollments due to other reasons. The boxplots in Figure 5.11 show the spread of these predicted disenrollments. The observed deaths, plan changes, and disenrollments due to other reasons are also shown in Figure 5.11 for reference.

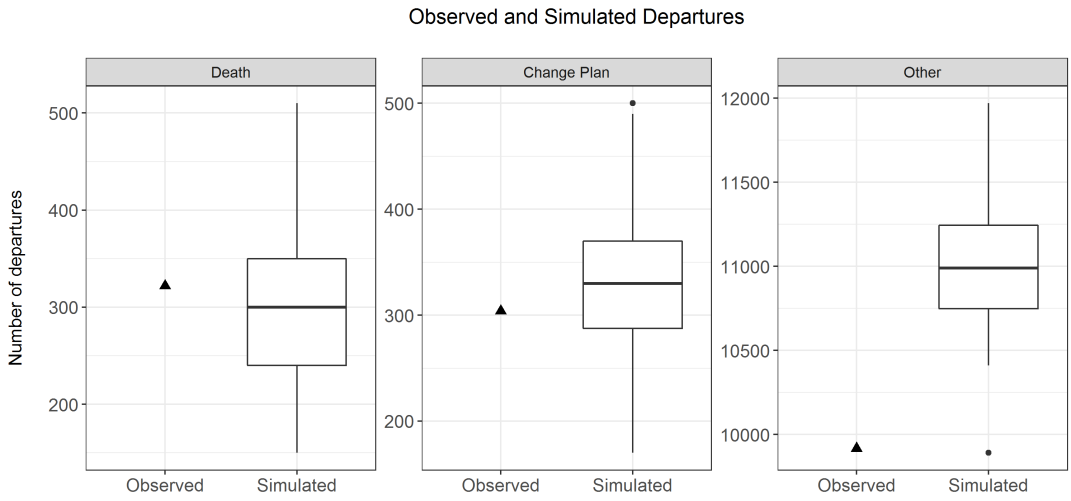

Figure 5.11: Simulated disenrollments by reason for disenrollment. Note that the y-axes are not the same in each panel.

5.3 Prediction of intervention effects

5.3.1 Intervention 1: Reduce Diabetes Effect

In our first intervention we reduce the effect of diabetes by 0-5% in both the health state and expenditure models. We obtain a surface of intervention effects for three outcomes of interest: (1) improvement in mean RUB score, (2) per member per month savings, and (3) annual savings.

5.3.1.1 Health State

If the effect of diabetes on health state and expenditure were reduced by 2.5%, we predict a mean improvement in RUB score of 0.02. There is no relationship between the mean improvement in RUB score and the percent change in diabetes effect on expenditure because the health state model precedes the expenditure model. The mean predicted improvement as well as the 2.5, 25, 75, and 97.5% quantiles of improvement are shown in Figure 5.12

5.3.1.2 Expenditure

We calculate both the PMPM savings and annual savings under intervention conditions (Figure 5.13, Figure 5.14). We see that directly reducing the effect of diabetes on expenditure reduces cost more rapidly than reducing the effect of diabetes on health state. For a 2.5% reduction in the effect of diabetes on both health state and expenditure, we predict a mean PMPM savings of $60 ($40-80). Across the entire population, this would amount to $15 million savings ($10-20 million).

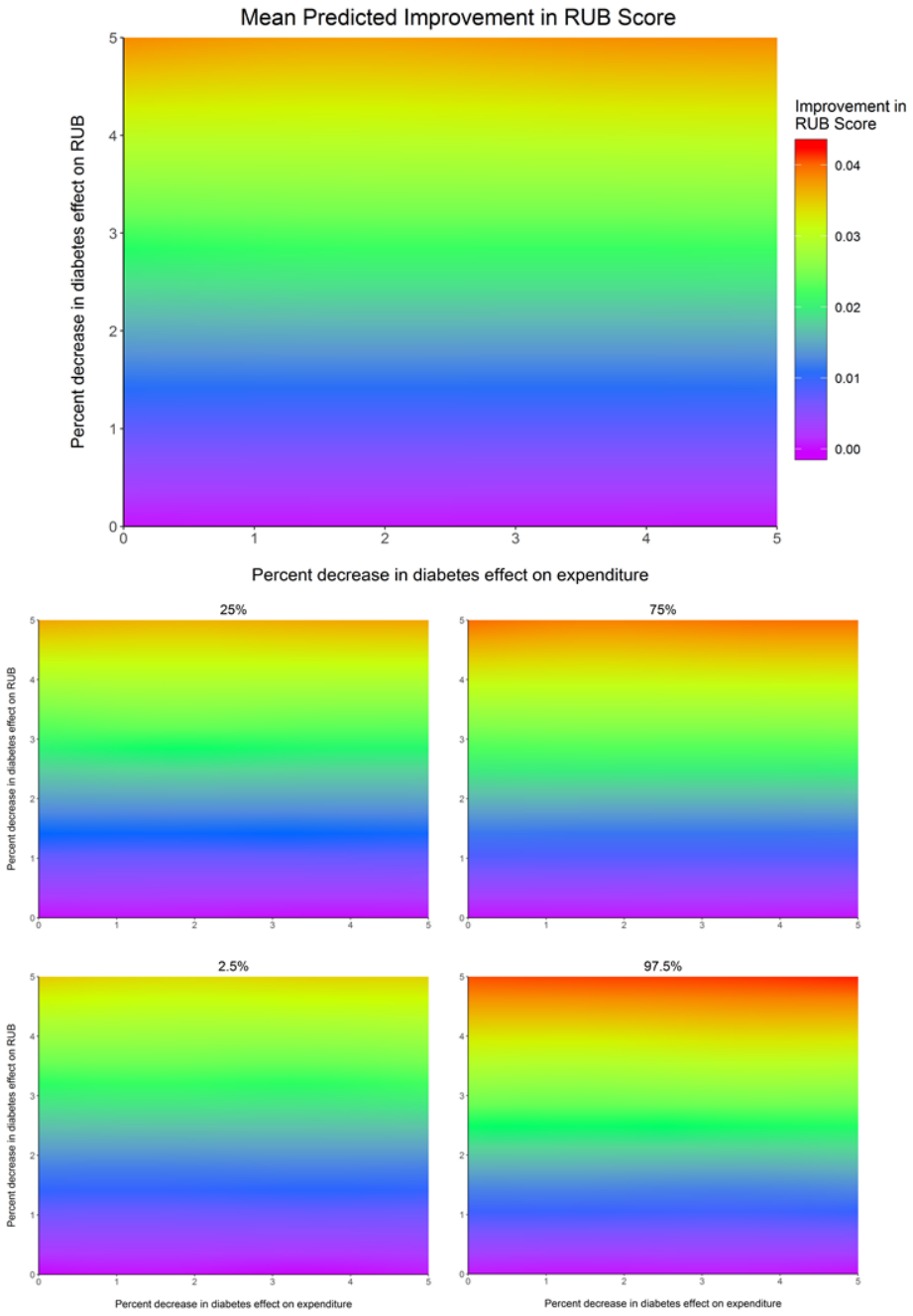

Figure 5.12: Predicted improvement in RUB score. The top panel shows the mean predicted improvement in RUB score. In the second row, the left and right panels show the 25 and 75% predicted improvement in RUB score, respectively. The lower left and right panels show the 2.5 and 97.5% predicted improvement, respectively.

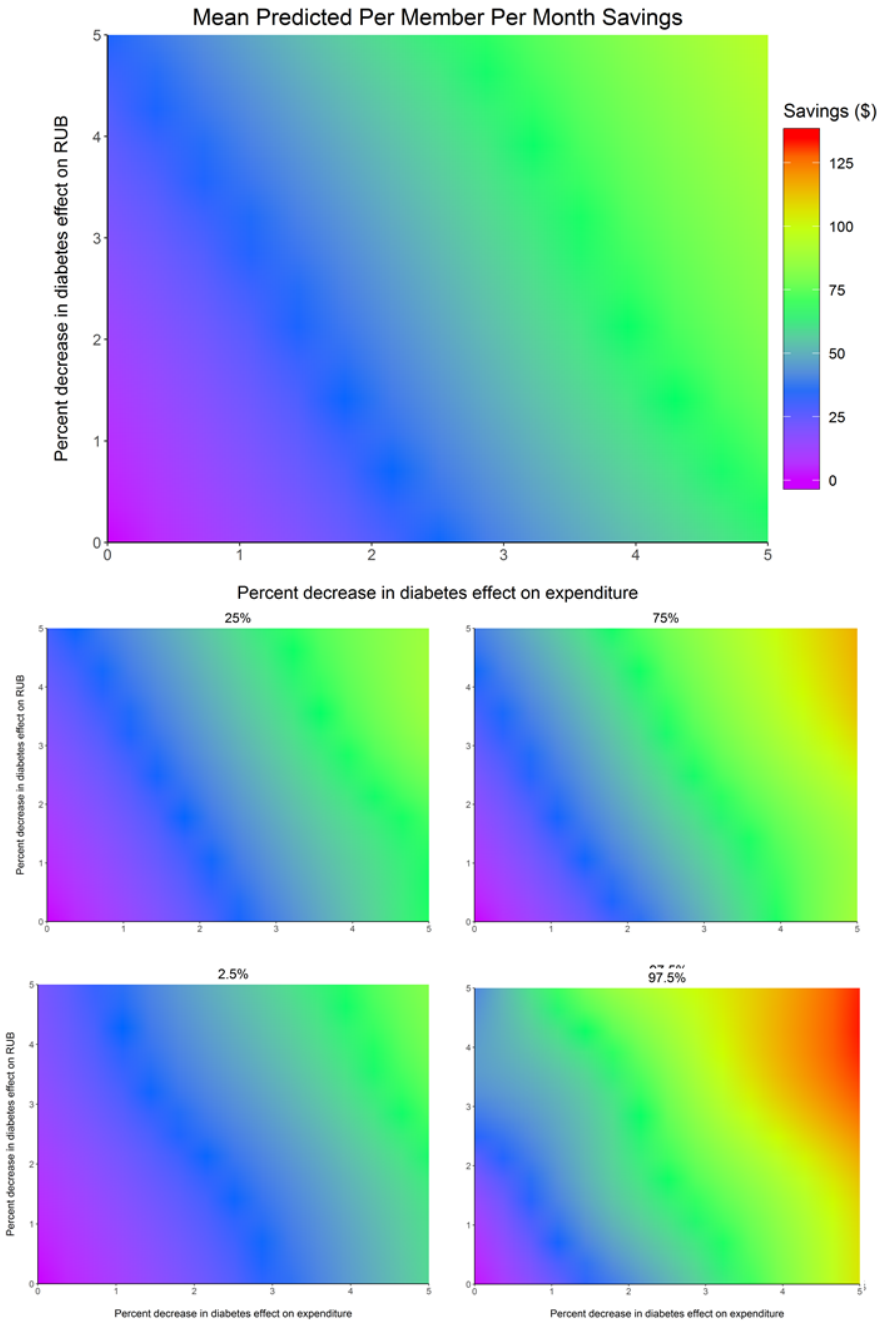

Figure 5.13: Predicted PMPM savings based on 10 simulations. The top panel shows the mean predicted savings. In the second row, the left and right panels show the 25 and 75% predicted savings, respectively. The lower left and right panels show the 2.5 and 97.5% predicted savings, respectively.

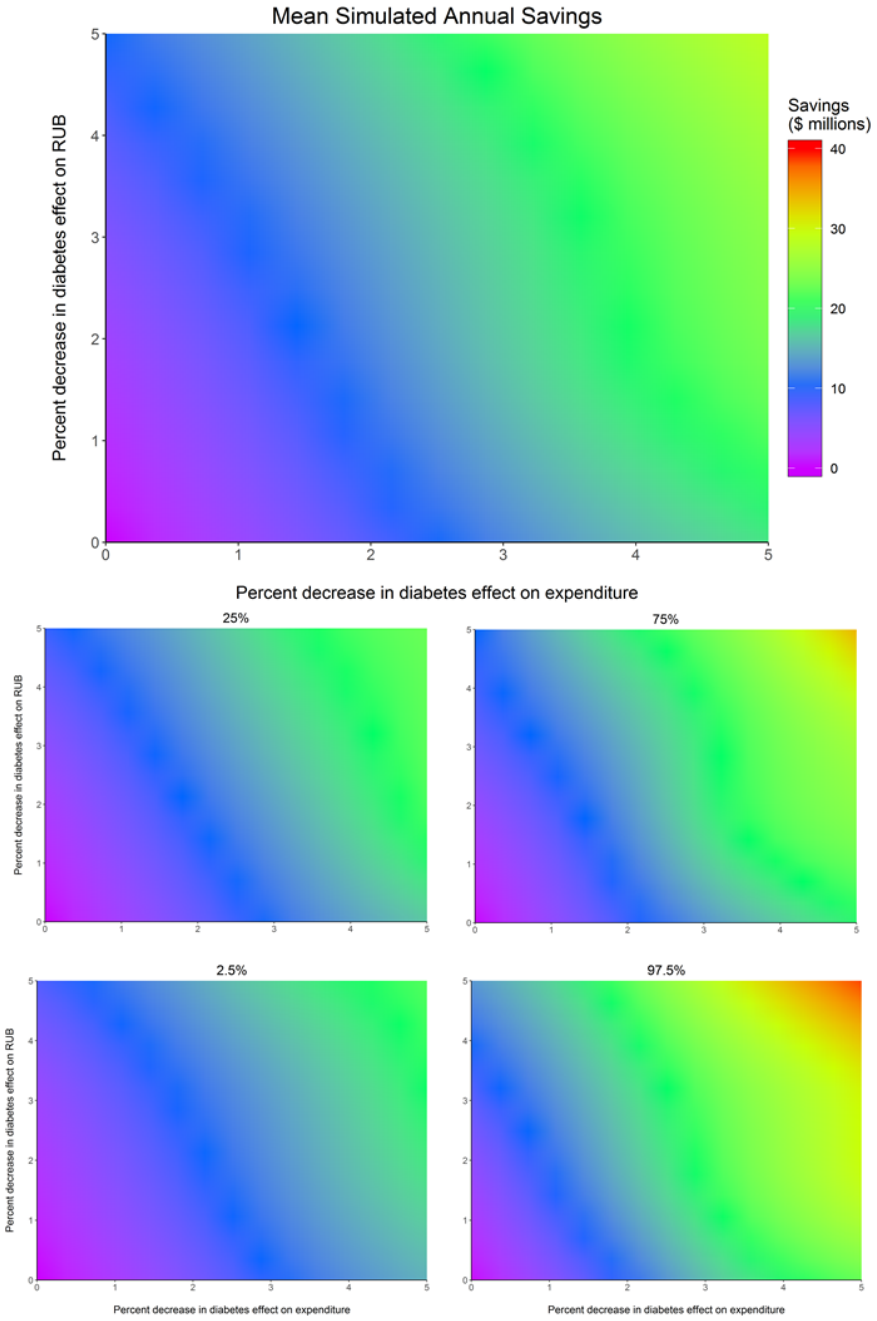

Figure 5.14: Predicted annual savings based on 10 simulations. The top panel shows the mean predicted savings. In the second row, the left and right panels show the 25 and 75% predicted savings, respectively. The lower left and right panels show the 2.5 and 97.5% predicted savings, respectively.

5.3.2 Intervention 2: Reduce Average Plasma Glucose

5.3.2.1 Expenditure

Recall our assumption of a causal relationship between HbA1c and medical expenditure (Lissovoy, Ganoczy, and Ray, 2000). In our second intervention we reduce the average plasma glucose concentration (HbA1c) by 0-1%[2] in all Medicare Advantage patients. We see a strong approximately linear relationship between the absolute reduction in HbA1c and the PMPM savings (Figure 5.15). If HbA1c is reduced by 0.7%, as in the DECIDE program,[3] we predict a PMPM savings of $200.

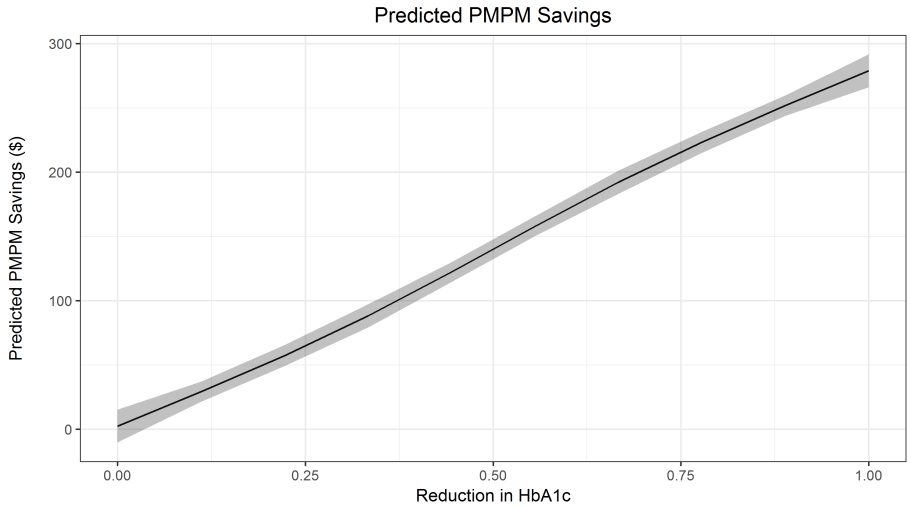

Figure 5.15: Predicted per member per month savings based on 10 simulations. The x-axis corresponds to absolute reduction in HbA1c (i.e. not percent reduction). The estimate shown here was obtained by regressing the predicted savings in our PIE model on a smooth function of the reduction in HbA1c. The shaded region is a 95% confidence band.

[2] 0-1% is an absolute (i.e. not percent) reduction in HbA1c. HbA1c is reported as a percent.

[3] DECIDE is a program run by Hopkins that provides online or in-person training to educate patients with Type 2 diabetes about lifestyle changes that can improve their clinical outcomes.

Chapter 6

Discussion and Conclusion

We propose a simulation-based approach to predicting intervention effects in healthcare systems, henceforth termed the Prediction of Intervention Effects (PIE) model. The approach can simulate the complex interplay between health, utilization, expenditure, and time. One strength of this approach is its flexibility; the basic framework can be expanded to incorporate additional component models as dictated by the problem of interest. Additionally, the component models can be manipulated separately or in conjunction with one another to estimate a variety of interventions. We use two interventions to illustrate the potential value of our PIE model.

6.1 Intervention case studies

6.1.1 Intervention 1: Reduce Diabetes Effect

In our first simulation, we reduce the effect of diabetes on health state and expenditure by 0-5%. We calculate (1) improvement in mean RUB score, (2) PMPM savings, and (3) annual savings.

Since health state does not depend on expenditure in our model, the mean improvement in RUB score is only a function of the reduction in the effect of diabetes on health state. If we reduce the effect of diabetes by 2.5%, we simulate a mean improvement in RUB score of 0.02 (0.1-0.3). This result makes intuitive sense because our health state model estimates that a diabetic patient will have a RUB score 0.82 units higher than an otherwise similar nondiabetic in women and 0.97 units higher than an otherwise similar nondiabetic in men. If we reduce each of these by 2.5% and take the average, we see an improvement in RUB score of 0.2. This is reflected in the simulated system.

For a modest reduction in the effect of diabetes on health state and expenditure (2.5% in both models), we predict a mean PMPM savings of $60 ($40-80) for diabetics. The PMPM savings is a valuable metric because certain subpopulations might more easily attain these margins of improvement. For example, a 2.5% reduction in the effect of diabetes on health state and expenditure in the subset of poorly-controlled diabetics might be more feasible than in the subset of diabetics who are already taking the necessary steps to minimize the burden of their disease. A pilot intervention that targets 2,500 diabetics with the goal of reducing the effect of their disease on health state and expenditure could save JHHC $150,000 annually.

If the effect of diabetes could be reduced by 2.5% in the *entire* population, we predict a mean annual savings of $15 million ($10-20 million). To realize these savings would require large-scale and thus potentially expensive interventions. Since the PIE model does not adjust for the cost of intervention deployment, the $15 million in savings would have to be interpreted in the

context of intervention cost. While not adjusted for intervention cost, the annual savings metric provides a sense of the potential impact an intervention could have when deployed plan-wide.

6.1.2 Intervention 2: Reduce Average Plasma Glucose

In our second simulation, we consider only Medicare Advantage patients. This subpopulation has the highest proportion of diabetic patients and the oldest age distribution out of the four lines of business. This combination makes MA patients some of the most expensive in the JHHC plan; consequently, interventions that could reduce their expenditure while improving their health are in high demand. One such intervention aims to reduce plasma glucose concentration (HbA1c) by 0.7%. We simulate reductions in HbA1c ranging from 0-1%.[1] We calculate PMPM savings and find that a 0.7% decrease in HbA1c would save approximately $200 per member per month. If 500 Medicare Advantage patients achieve this level of improvement, it could save $1.2 million over the course of a year. If the 3,578 diabetic members in Medicare Advantage achieve this level of improvement, it could save $8.6 million.

Since the MA patients tend to be older and sicker than the rest of the JHHC population, we do not think this result can be generalized to other lines of business; we suspect the PMPM savings in other lines of business would be lower.

[1] 0-1% is an absolute (i.e. not percent) reduction in HbA1c. HbA1c is reported as a percent.

6.2 Future model improvements

6.2.1 Enrollment

Our enrollment models currently smooth outcomes of interest over the state of Maryland. However, beyond identifying interesting spatial patterns, these results are not incorporated into the analysis. This aspect of our current approach restricts the types of interventions that can be simulated. There is value to refining these models such that questions pertaining to *who* enrolls in the plan can be investigated. We hope to provide the flexibility to allow geographic studies of who enrolls by ZIP code to inform evaluation of JHHC marketing strategies. This modeling approach can also be used to assure and document JHHC's compliance with regulations about access to their plans.

In addition to modeling enrollment into JHHC, we can model enrollment into particular interventions. By incorporating spatial data into our analyses, we can identify regions rich in poorly-controlled diabetics or those with deteriorating health states; relevant interventions could be more aggressively targeted to these regions. Understanding the spatial distribution of disease could be especially valuable in cases where part of a proposed intervention is administered in-person. A pilot intervention could be deployed specifically in the region identified as having the greatest potential for improvement.

6.2.2 Health State

Health state is unobservable but can be approximated using clinical and claims data. For example, we might be confident that an individual is a diabetic if they

have (1) multiple plasma glucose readings that place them above the threshold for diabetes, and (2) regular prescription claims for insulin. However, there are less clear-cut cases, especially when the patient interacts infrequently with the healthcare system. Infrequent utilization of health services could be indicative of a healthy patient or a patient with poorly monitored and managed conditions.

The problem of assigning each patient a time-varying health state becomes even more complicated when we consider possible combinations of comorbidities as well as variable behavior with respect to disease control (e.g. two patients might have diabetes and COPD diagnoses but behave very differently with respect to managing these conditions; these patients, though sharing the same diseases, do not share a health state). We have been using RUB score as a crude estimate of health state. It has always been a placeholder for a better health state variable. We plan to move our PIE model into PMAP so we can take full advantage of the rich clinical data in this platform. We plan to improve our health state model by using restricted latent class models (Wu et al., 2019).

6.2.3 Expenditure

We currently have expenditure data aggregated to the monthly level (i.e. PMPM expenditure). We hope to decompose the monthly expenditure data into utilization and expenditure data. We believe that the pattern of utilization is as important as the absolute number of dollars spent. Two patients with the same PMPM expenditure could have very different underlying health states that are not adequately captured by an amount spent in a given month.

For example, one could have a large expenditure from a one-time emergency room visit and the other could have a series of medium-cost expenditures due to a chronic condition. The health state and expenditure trajectories of these two patients should be very different even though their PMPM expenditure might be the same.

6.3 Future directions

6.3.1 Individual prediction

With the aforementioned improvements to the health state measure we will develop and implement a method to predict patient trajectories. If fully incorporated into the PMAP system, the method can capitalize on the clinical data therein. We envision the health state trajectory being dynamic in that it will update as new data are entered into PMAP. This predicted trajectory could function as a tool to identify patients who require intervention; if identified early, patients can realize their maximum benefit and avoid deteriorating into a health crisis.

6.3.2 Population prediction

We plan to develop a user-friendly interface such that these models can support evidence-based decision making. We want the PIE model to be flexible enough that a wide variety of interventions could be evaluated for their ability to improve population health at affordable costs. In the short-term, we plan to develop a Shiny App that allows the user to adjust the model inputs (e.g. HbA1c data vs. RUB score) and specify the change they want to make to one

or more of the variables in one or more of the component models (e.g. reduce HbA1c by 0.5% and reduce the effect of diabetes on expenditure by 2%).

6.4 Conclusion

Medicine has advanced beyond measure in the past few centuries, with such milestones as the discovery of antibiotics and the advent of vaccines. Many diseases and conditions that were formerly thought to be death sentences are now preventable or treatable. However, as remarkable as the current state of medicine is, there is still work to be done. Healthcare expenditure in the US has grown unsustainably while measures of health quality have stagnated. Many of the life-changing health innovations are inaccessible to the patients who need them most due to health inequality and prohibitive costs. There is an urgent need to reduce waste in national healthcare expenditure. One approach to identifying cost-effective solutions is precision medicine.

Precision medicine is evidence-based, patient-focused, and necessarily dynamic. It is built around the fundamental idea of allowing health data to speak for themselves and inform the most appropriate monitoring, treatment, and intervention plans for subpopulations of individuals with shared characteristics. Precision medicine can act at various levels of granularity, from genetic and genomic data to population data. Whether the proximal goal is a treatment and monitoring regimen, or evaluation of the most cost-effective and beneficial interventions, the ultimate goal of precision medicine is to present patients with the best supported and most beneficial plan *for them*.

We have both the data and the demand for the development of more efficient and better targeted healthcare strategies. Shown here, we predict intervention effects at the population level. We propose our PIE model as a decision-support tool to quantitatively evaluate the relative merits of different interventions. It is a flexible framework that can accommodate varied scenarios. We will continue to refine the model through collaboration with others who share our goal of improving population health at more affordable costs.

Chapter 7

Appendix

7.1 Smearing coefficient results

Since we model expenditure on the log scale, we have to multiply by the smearing coefficient when we retransform our predicted values from log dollars to dollars. This is to adjust for the skewness in the observed expenditure data. There is some heterogeneity in the predicted smearing coefficient by RUB, diabetes status, and age. The smearing coefficient increases with increasing RUB score in both diabetic and non-diabetic patients, though the spread is much more pronounced in non-diabetic patients. We see it decrease with age in the non-diabetic patients and remain relatively stable in the diabetic patients (Figure 7.1).

7.2 Expenditure model results

We find that predicted expenditure is largely unrelated to increasing age after stratifying by diabetes diagnosis and RUB. We return to the original data to confirm that our models reflect observed patterns in the JHHC population.

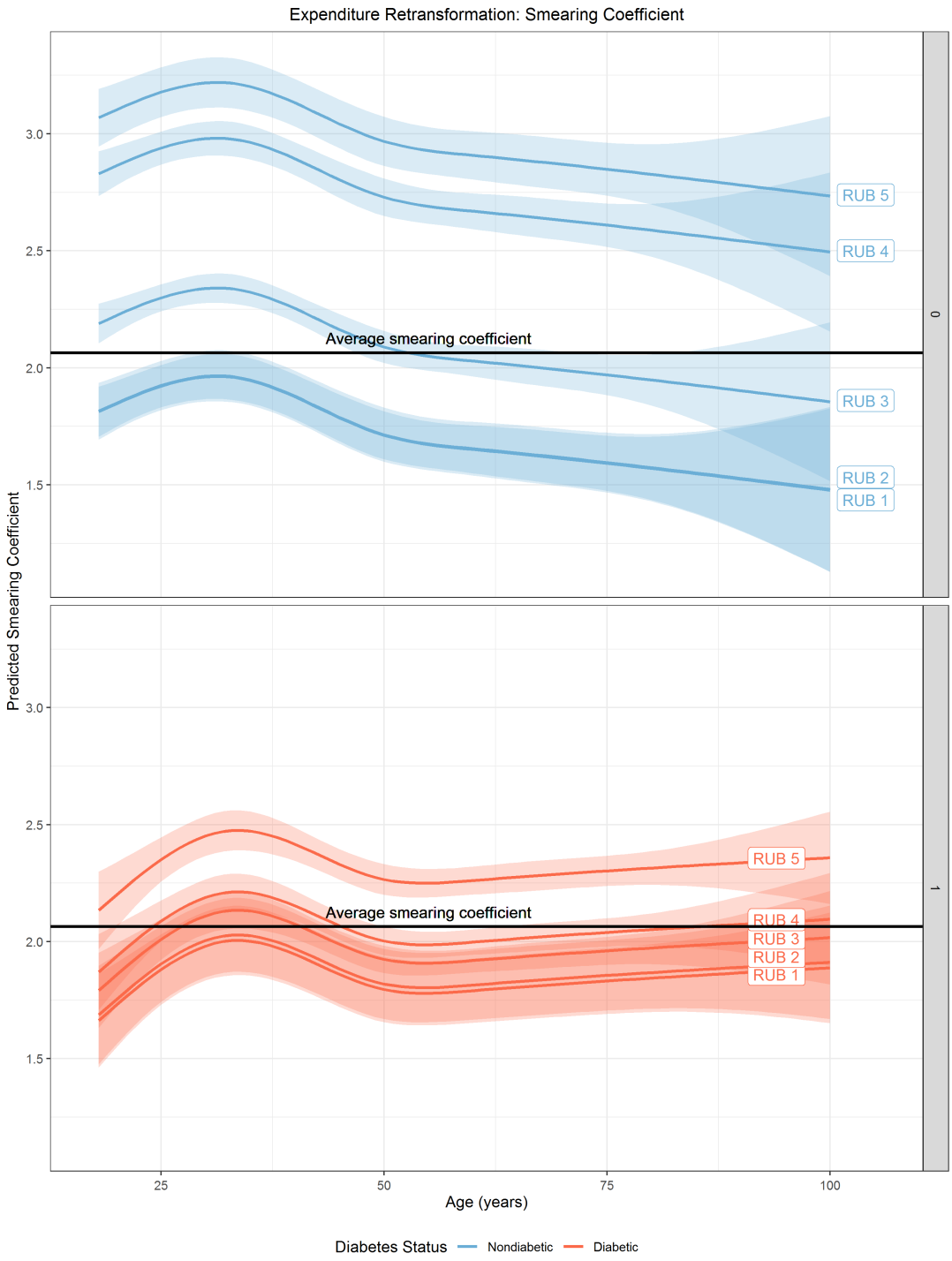

Figure 7.1: Smearing coefficient by RUB score, age, and diabetes diagnosis.

Recall that there is a strong positive association between age and RUB score (Figure 3.3, Figure 5.3); patients in higher age strata tend to have higher RUB scores. We also see a strong positive association between RUB score and PMPM expenditure (Figure 7.2). Thus, old patients tend to have high RUB scores and consequent high expenditure. To confirm that there is minimal effect of being old above and beyond that explained by health state, we look at observed PMPM expenditure stratified by diabetes status, age, and RUB score (Figure 7.3). In keeping with our model results, PMPM expenditure is largely stable across the age strata.

Figure 7.2: Observed PMPM expenditure by RUB score.

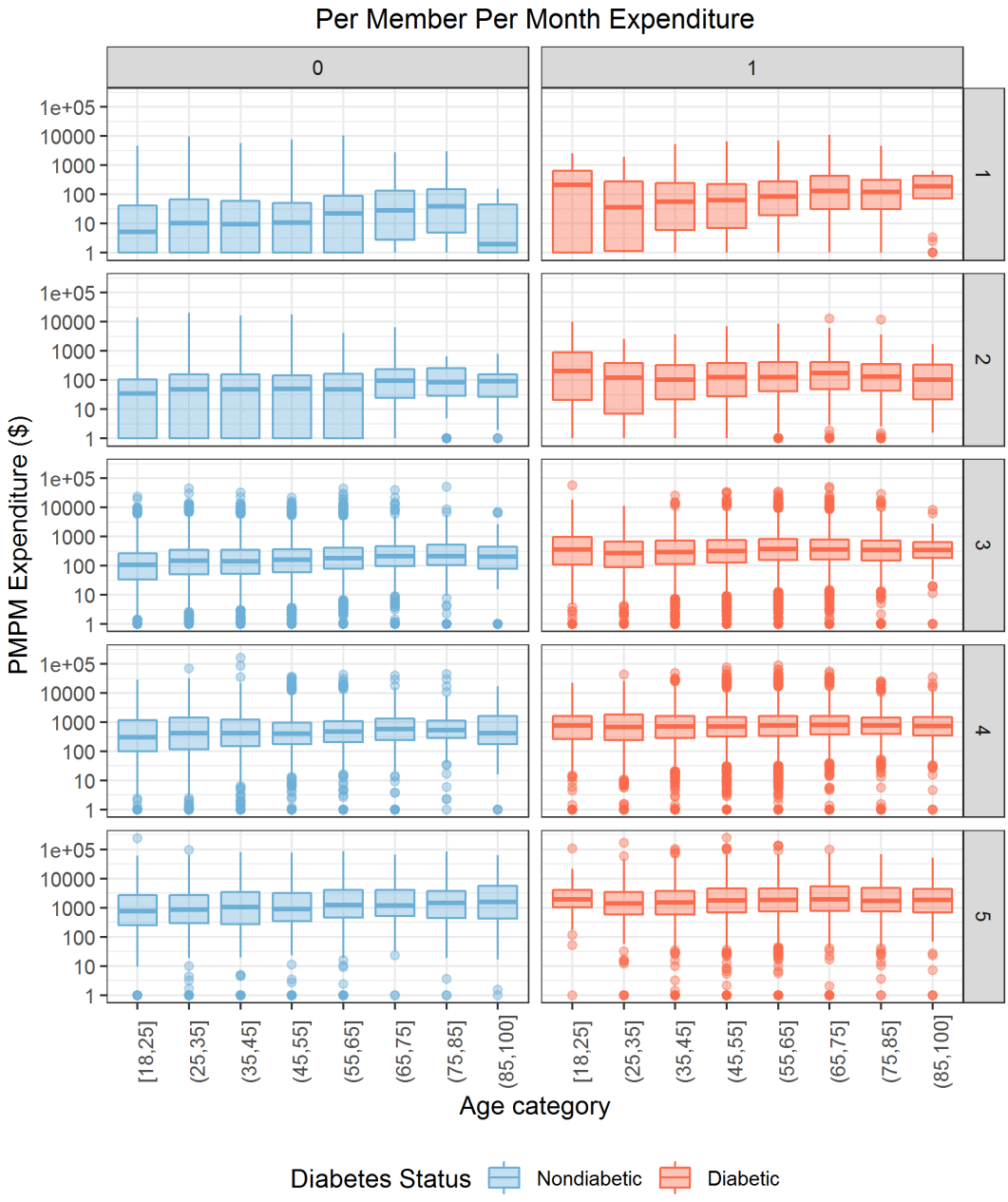

Figure 7.3: PMPM expenditure by RUB score and Age. The RUB scores are shown in the banners on the right of each plot. The top row corresponds to RUB score 1 and the bottom row corresponds to RUB score 5.

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Education

2017-2019 **ScM** in **Biostatistics**, *May 2019 (anticipated)*
Johns Hopkins Bloomberg School of Public Health, *Baltimore, MD*
- Thesis title: *Prediction of Intervention Effects in Health Systems: Johns Hopkins HealthCare Diabetes Case Study*
- *GPA: 3.95*

2012-2016 **BS** in **Mathematical Biology** and **Biological Sciences** (double major), *December 2016*
University of Pittsburgh, *Pittsburgh, PA*
- Chancellor's Scholar
- *Summa cum laude*, *GPA: 3.75*

Biostatistics Research Experience

June 2018 – present **Johns Hopkins inHealth Biostatistician and Data Analyst**, *Baltimore, MD*
Adviser: Scott Zeger, Ph.D., Johns Hopkins Dept. of Biostatistics
- Analyze Johns Hopkins HealthCare administrative and clinical data to investigate:
  - Plan members' health states and health state trajectories
  - Optimal interventions to improve population health at more affordable costs
- Skills: R, regression, survival analysis, machine learning

Jan. 2017 – present **Research Associate**, National Aviary, *Pittsburgh, PA*
Adviser: Nathan Brouwer, Ph.D., Dept. of Conservation and Field Research
- Work to better understand how populations of migratory birds change over time
- Analyze longitudinal population survey data
- Skills: R, generalized linear mixed models, population simulation

Additional Professional Experience

Sept. 2015 – Apr. 2016 **Ophthalmic Technician** ▪ Guerrilla Eye ▪ University of Pittsburgh School of Medicine
Adviser: Attending physician by clinic day
- Travel to local free clinics and provide eye exams
- Take medical history, provide basic eye exam, and present case to attending physician
- Skills: Patient interaction, refraction, dilation, tonometry

July – Aug. 2015 **Field Technician**, Northeast Ecological Services, *Galloo Island, NY*
Adviser: D. Scott Reynolds, Ph.D.
- Survey via acoustic monitoring to evaluate the presence of endangered bat species in potential construction sites
- Survey via mist netting to better understand potential consequences to local bat population of wind farm installation
- Skills: Mist netting, acoustic monitoring, animal handling

Feb. – Dec. 2014 **Undergraduate Researcher**, University of Pittsburgh School of Medicine, *Pittsburgh, PA*
Adviser: Paul R. Kinchington, Ph.D., Dept. of Ophthalmology
- Created two Shingles virus mutants to investigate the role of two proteins (ORF4p & ORF9p) in chronic Shingles-related pain in a rat model
- Characterized viral growth curves *in vitro* for the two viral mutants
- Training: Chemical Hygiene, Bloodborne Pathogens, IACUC
- Skills: PCR, qPCR, cell culture, protein purification, animal handling and harvesting, virus amplification, recombination

Jan. – Apr. 2013 **Undergraduate Researcher**, University of Pittsburgh School of Medicine, *Pittsburgh, PA*
Adviser: Elane Fishilevich, Ph.D., Department of Developmental Biology
- Undergraduate Researcher through the *First Experiences in Research* Program
- Investigated efferocytosis in fruit fly (*Drosophila melanogaster*) cell culture using a pH-sensitive GFP reporter to monitor cell engulfment
- Skills: PCR, cell culture, imaging, microscopy, primer design

Presentations

Oct. 2018 **E.A. Scott**, N.L. Brouwer, S.C. Latta, B.A. Tinoco, P.X. Astudillo, C.H. Graham. Is Avian Biodiversity at Risk in the tropical Andes? 10-year monitoring study results. Student Conference on Conservation Science. American Museum of Natural History, NYC, NY.

Sept. 2017 N.L. Brouwer, **E.A. Scott**, S.C. Latta. Making the most of your data: Advantages of mixed-effects models for the analysis of complex data. Three Rivers Evolutionary Event (TREE), University of Pittsburgh, Pittsburgh, PA.

Dec. 2014 **E.A. Scott**, J.M. Guedon, and P. Kinchington. VZV ORF9 Contributions to Pain: ORF9 E85R & ORF9 S84A E85R Mutants. University of Pittsburgh School of Medicine, Pittsburgh, PA.

Dec. 2014 **E.A. Scott**, J.M. Guedon, and P. Kinchington. *In vitro* Characterization of ORF4 and ORF29 Mutants. University of Pittsburgh School of Medicine, Pittsburgh, PA.

Apr. 2013 **E.A. Scott**, M. Krajcovic, S. Headland, and E. Fishilevich. The Role of *Drosophila* Matrix Metalloproteinases in Efferocytosis. First Experiences in Research Poster Symposium. University of Pittsburgh, Pittsburgh, PA.

Dec. 2012 **E.A. Scott**, M. Ward. A Brush with Electrochemistry. Analytical Chemistry Annual Poster Session. University of Pittsburgh, Pittsburgh, PA.
Poster was awarded 2nd place prize

Teaching Experience

Sept. – Dec. 2018 **Graduate Teaching Assistant** ▪ Johns Hopkins University Whiting School of Engineering
- EN.500.111.34 HEART: Foundations of Statistical Machine Learning
- Attend lectures and provide students with in-class support while instructor leads machine learning projects

Aug. – Dec. 2018 **Graduate Teaching Assistant** ▪ Johns Hopkins University Dept. of Public Health Studies
- AS.280.345 Public Health Biostatistics
- Teach 50-minute lab section once per week and hold office hours

Sept. 2013 – Apr. 2016 **Math Assistance Center Tutor** ▪ University of Pittsburgh Dept. of Mathematics
- One-on-one tutoring in Algebra, Trigonometry, Calculus 1, 2 & 3, Linear Algebra

June – Jul. 2015 **Molecular Biology Teaching Intern** ▪ St. Paul's School
- Advanced Studies Program (ASP) Molecular Biology Teaching Intern
- Taught a class of 13 rising senior high school students topics in molecular biology
- Lectured, supervised labs, coached swimming and cross country, and served as a Resident Assistant

Sept. 2013 – Dec. 2014 **Undergraduate Teaching Assistant** (UTA) ▪ University of Pittsburgh Dept. of Mathematics
- MATH 0032 Trigonometry and Functions UTA (Fall 2014)
- MATH 0031 College Algebra UTA (Spring 2014)
- MATH 0200 Preparation for Scientific Calculus UTA (Fall 2013)

Honors and Awards

2016	**Record of Achievement** ▪ CAPA The Global Education Network ▪ Sydney, Australia Awarded in recognition of outstanding academic achievement in the study abroad program.
2012 – 2016	**Chancellor's Scholarship** ▪ University of Pittsburgh ▪ Pittsburgh, PA Awarded to 5 entering first-year undergraduates. Includes full tuition, room and board for four years of study. The most prestigious award offered by the University.
2013 – 2016	**University Honors College Ambassador** ▪ University of Pittsburgh ▪ Pittsburgh, PA Position awarded to students active in University Honors College (UHC) activities. Responsibilities include raising awareness within the University of Pittsburgh community about UHC programs, research fellowships, and events.
2013	***First Experiences in Research*** **Undergraduate Researcher** ▪ University of Pittsburgh Office of Undergraduate Research ▪ Pittsburgh, PA
2012	**2nd Place at the Annual Analytical Chemistry Poster Session** ▪ University of Pittsburgh Department of Chemistry ▪ Pittsburgh, PA

Computing Skills

- **Advanced:** R, Microsoft Office
- **Intermediate:** MATLAB, Adobe Photoshop and InDesign
- **Novice:** SAS, Java